CONTENTS

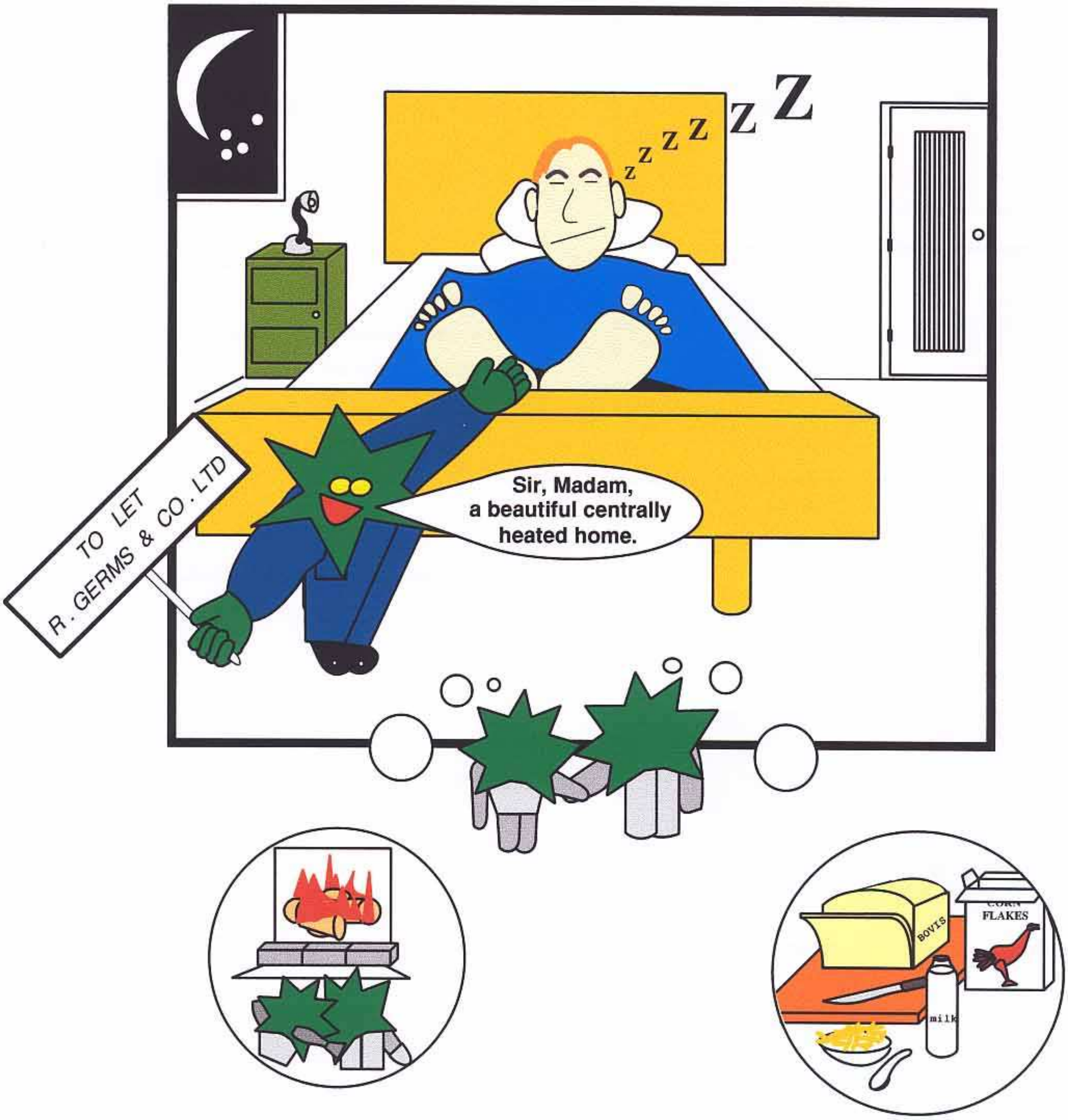
AN ILLUSTRATED GUIDE TO
THE IMMUNE SYSTEM

BY
JOSEPH LOCKYER

CHAPTER ONE

MEETING OUR FRIENDS AND ENEMIES

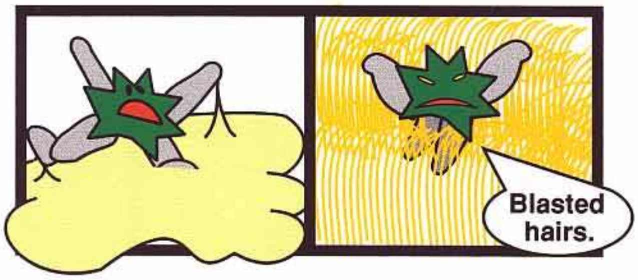
MICROBES



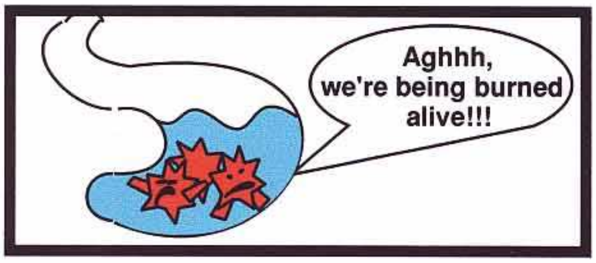
Unfortunately, this estate agent just happened to forget to mention that it is very difficult to get in!

WHAT STOPS MOST MICROBES GETTING IN?

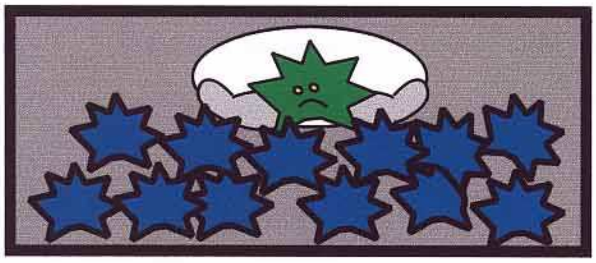
Intact skin acts as a barrier.



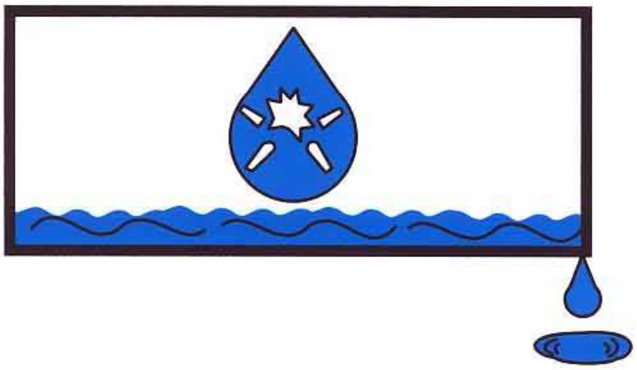
Sticky mucus and tiny hairs called "cilia" protect the airways.



Stomach acid sterilises our food.

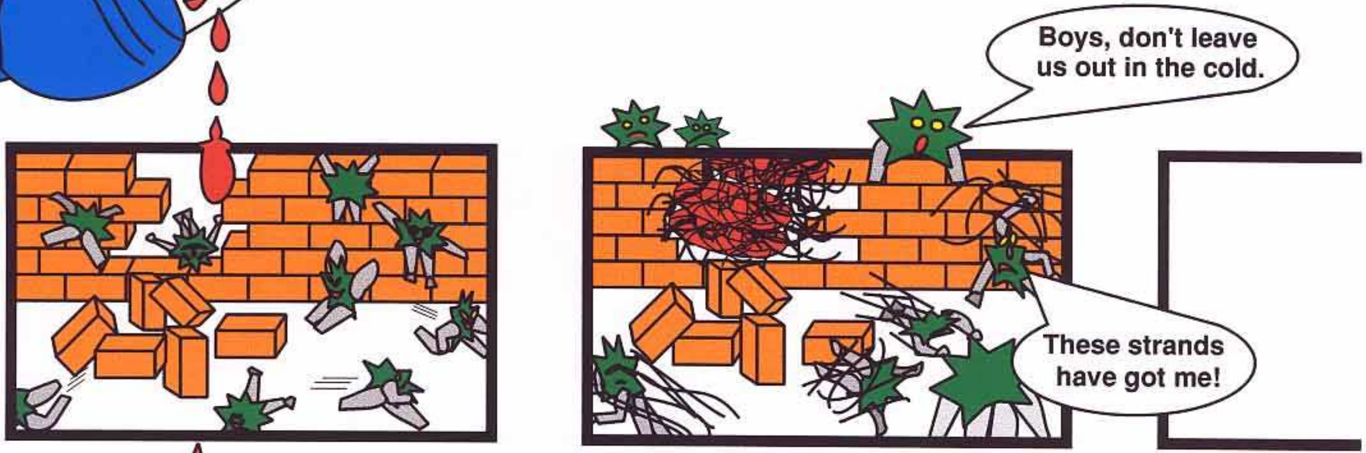


Because friendly commensal bacteria live inside our bodies, pathogenic bacteria (which could cause illnesses), are kept out.



Enzymes in tears will kill some bacteria.

AN INFECTED CUT



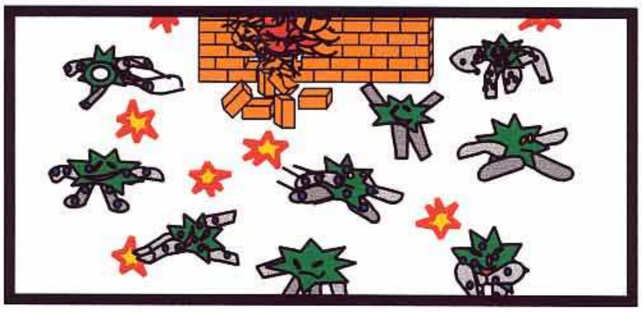
Although microbes pour through the cut, a blood clot quickly seals off the danger.

Easy reading

Technical information

The fibrin strands shown above, form in blood to help it clot and to ensnare foreign material.

THINGS GET WORSE

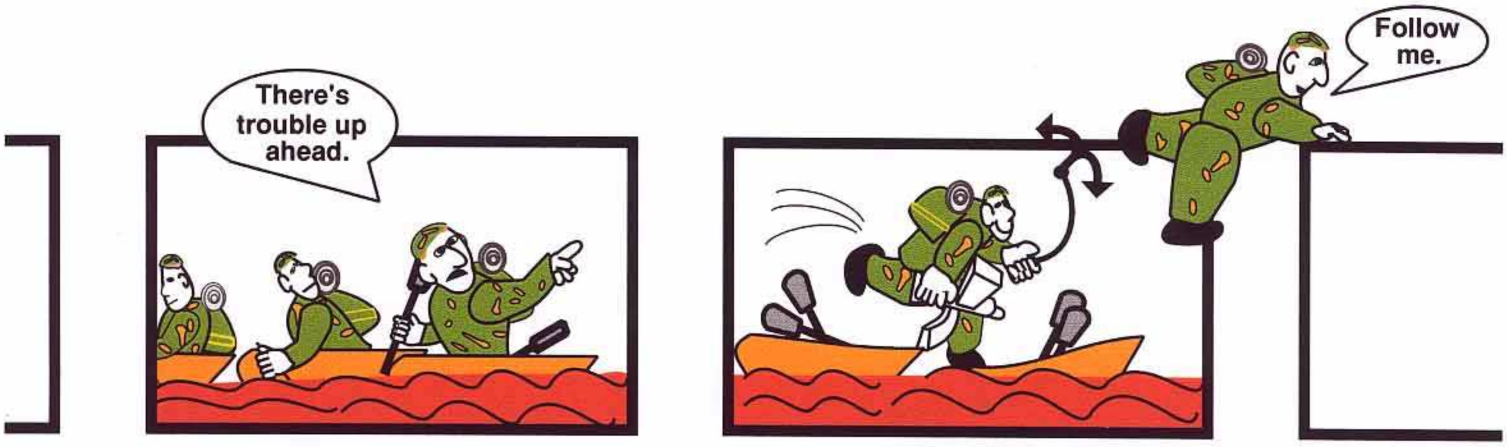


Despite the fibrin and inflammation released by activated complement, the microbes start to multiply and infect the locality.

COMPLEMENT

Complement (a group of immune chemicals), is rapidly activated when it comes into contact with a microbe.

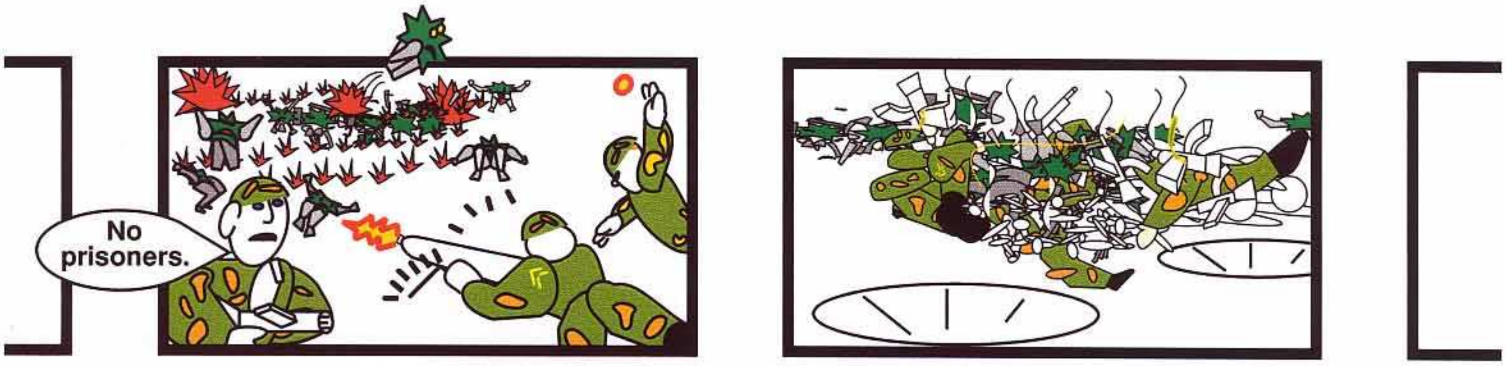
NEUTROPHILS



Meanwhile (in a nearby blood vessel), these neutrophils detect activated complement and realise they must leave the blood vessel, to see if they are needed.

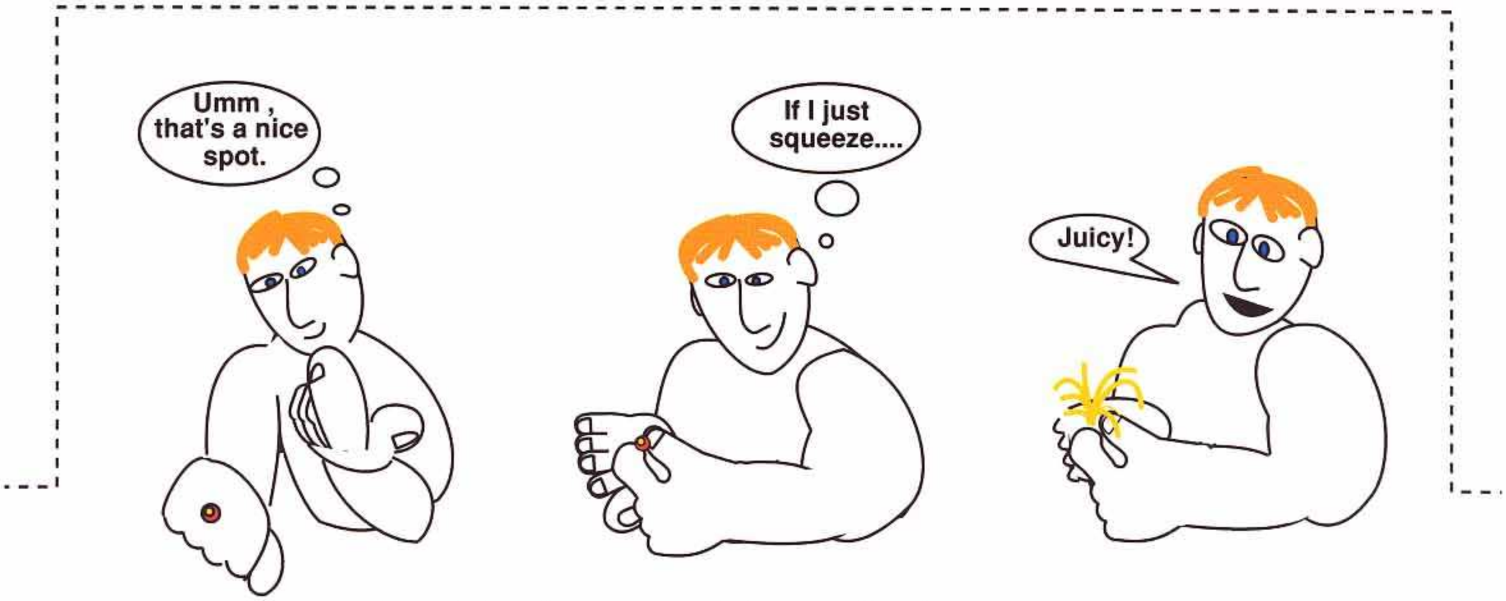
Neutrophils circulate around the body in the blood, ready to respond quickly, when the need arises.

LIFE IS JUST ONE BIG BATTLE FOR SURVIVAL



Emerging from the blood vessel, the neutrophils blow the microbes away!!

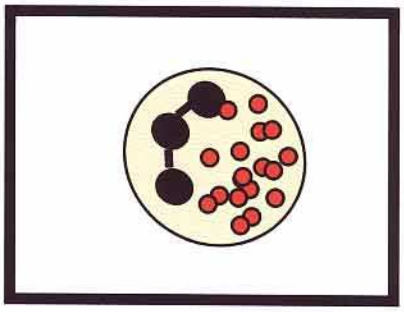
Soon it is all over, but many dead neutrophils now litter the war zone.



Suprisingly, pus that spurts from a spot, is mostly made up of dead neutrophils.

A PERSONAL PROFILE OF A NEUTROPHIL (PART 1)

Although the neutrophil is the commonest white blood cell, it only lives for about 2 days.

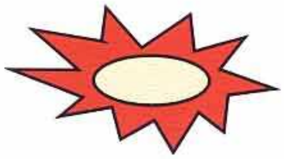


It has a multi-lobed nucleus and can contain up to 200 granules.

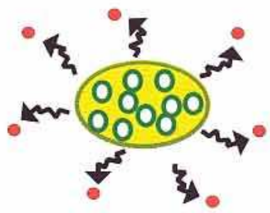
WHAT ATTRACTS A NEUTROPHIL?

Other immune cells

Traces of bacteria



Heat damaged cells

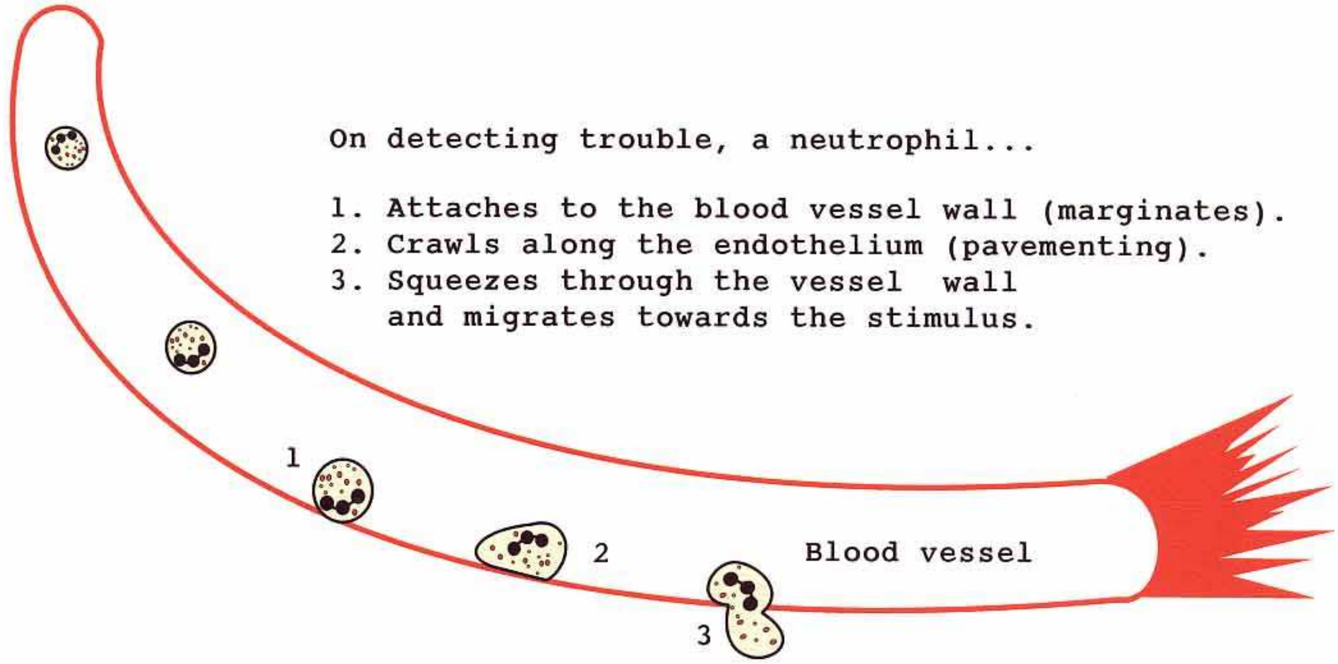


Complement activation

A PERSONAL PROFILE OF A NEUTROPHIL (PART 2)

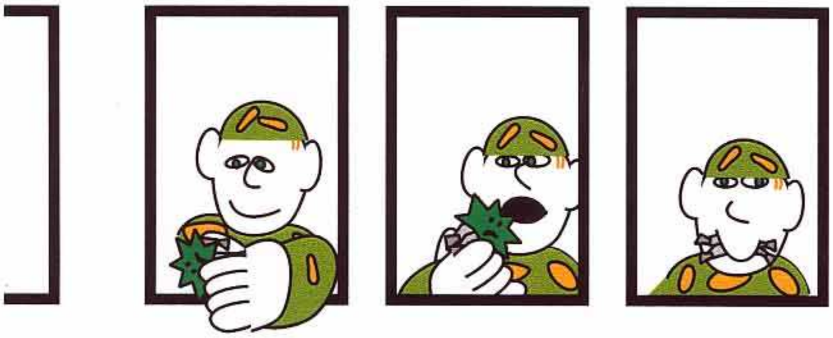
On detecting trouble, a neutrophil...

1. Attaches to the blood vessel wall (marginates).
2. Crawls along the endothelium (pavementing).
3. Squeezes through the vessel wall
   and migrates towards the stimulus.



Neutrophils can function in places where there is little oxygen, through carrying energy reserves (glycogen).

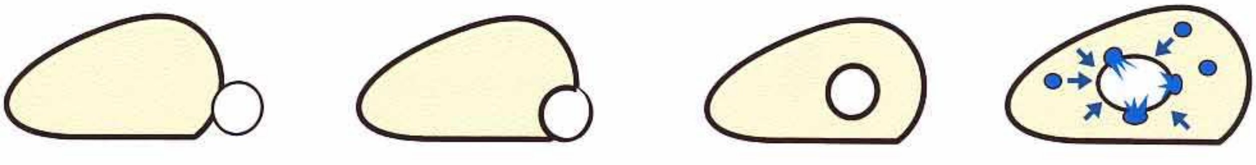
HOW NEUTROPHILS KILL INVADING BACTERIA



Neutrophils kill microbes by 'eating' and 'digesting' them.

To complete the job, inflammatory mediators are also released.

HOW A NEUTROPHIL 'EATS' AND 'DIGESTS' A MICROBE



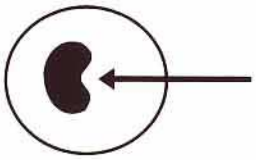
Attaching onto its prey, the neutrophil's membrane folds around the microbe, as it is drawn inside. The package now has a battery of toxic chemicals emptied into it, to kill and digest the intruder.

THE MONOCYTE

This young monocyte has just left the bone marrow.

After only a short time, he is welcomed into his new home.

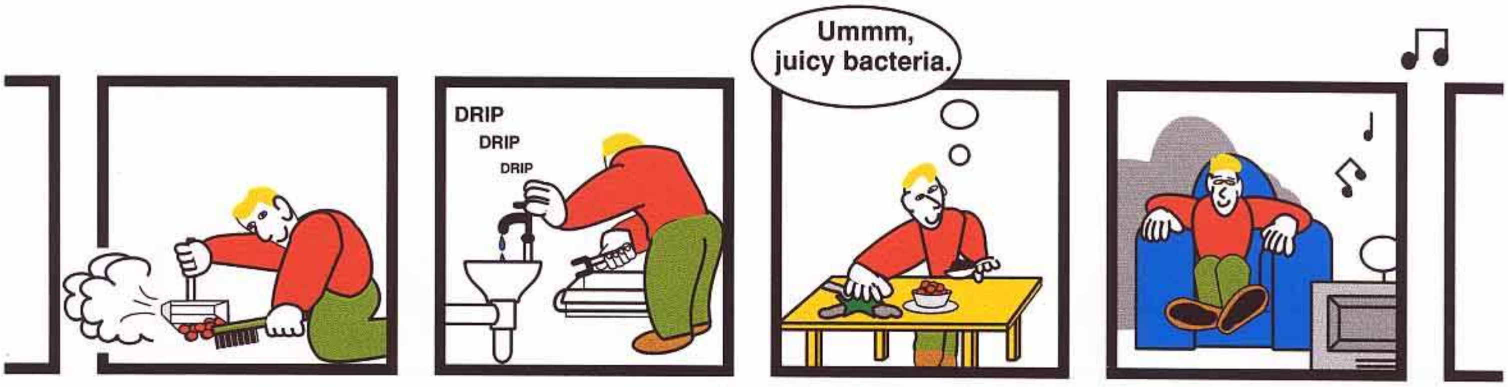
Here, he will become an adult macrophage.



Monocytes have a bean-shaped nucleus.

A monocyte starts life in the bone marrow. It then enters the blood and circulates around the body. After about 30 hours, the monocyte will migrate into the tissues and develop into a macrophage.

MACROPHAGES



Unlike the adventurous neutrophils, macrophages are happy just staying put and keeping their home tidy.

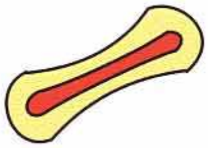
Macrophages are found all over the body. Their job is to remove waste and to facilitate new growth and development.

THESE MACROPHAGES SUDDENLY FIND THERE IS PLENTY TO DO

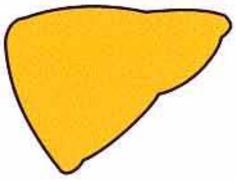
"Typical" said a macrophage, "those neutrophils are always leaving the place in a complete mess"!

However, it was not long before they had cleared away the dead and got things back to normal.

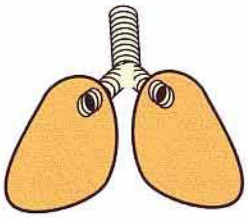
3 EXAMPLES OF WHERE MACROPHAGES ARE FOUND



Macrophages in bone, are called "osteoblasts".



Macrophages in the liver, are called "kupffer cells".

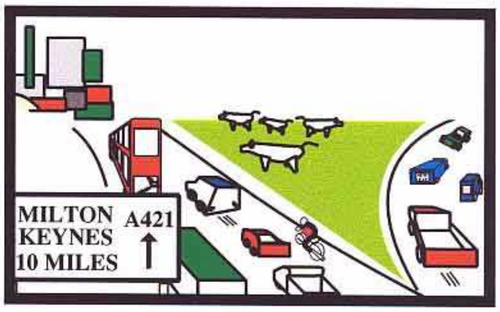


While in the lungs, these cells are called "alveolar macrophages".

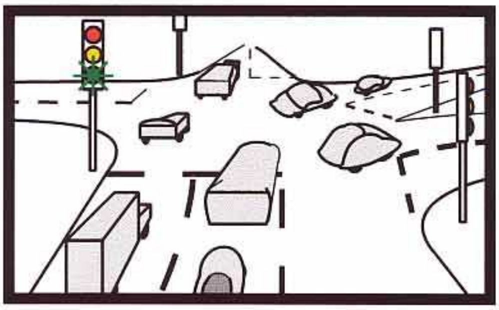
IF OUR BLOOD IS RED, WHY ARE WE BLACK OR WHITE AND NOT RED?

Roads give us a clue.

Just like most days, a large volume of traffic is pouring out of London.

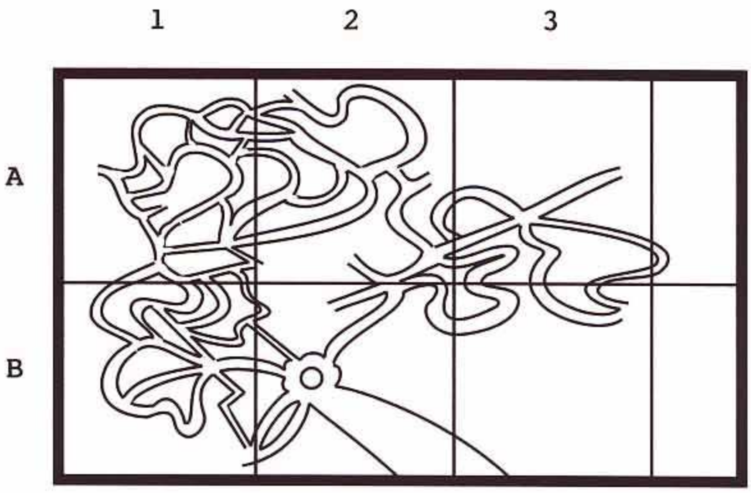


Travelling along the busy motorway, vehicles filter off onto smaller roads as they approach their destination.



"Welcome to Milton Keynes".

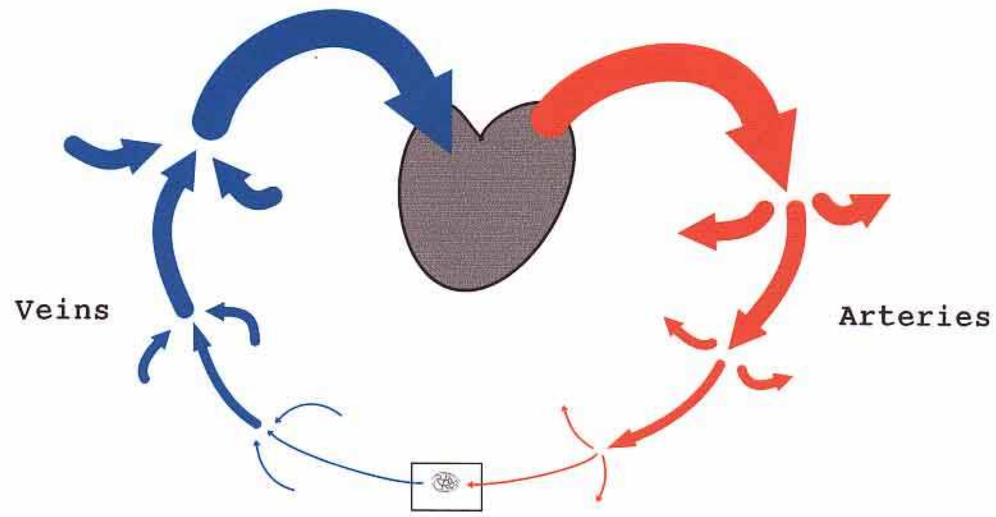
In the town, traffic moves much more slowly. Lorries deliver goods and people leave their cars to shop in the narrow side streets.



This local street map, shows how a trunk road, can quickly branch into hundreds of tiny town streets.

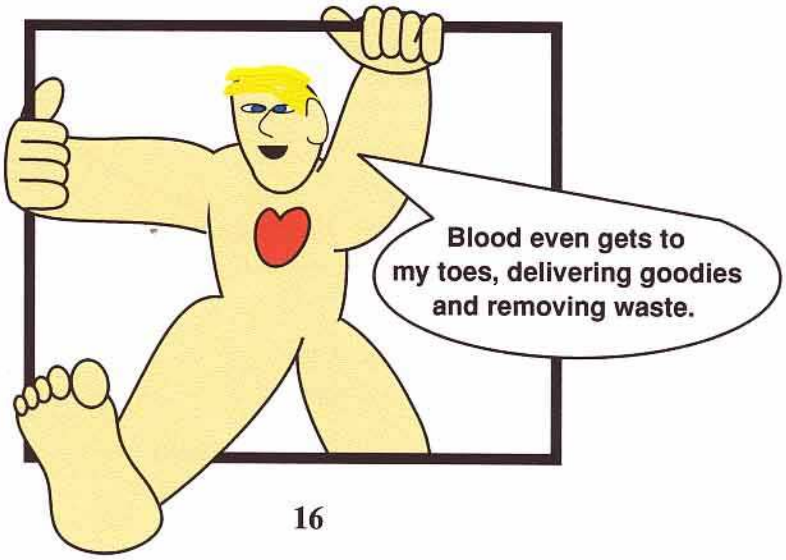
THE CIRCULATION

Blood is pumped around the body in arteries and then returns to the heart via the veins. Note how both the arteries and the veins divide into narrower and narrower vessels.

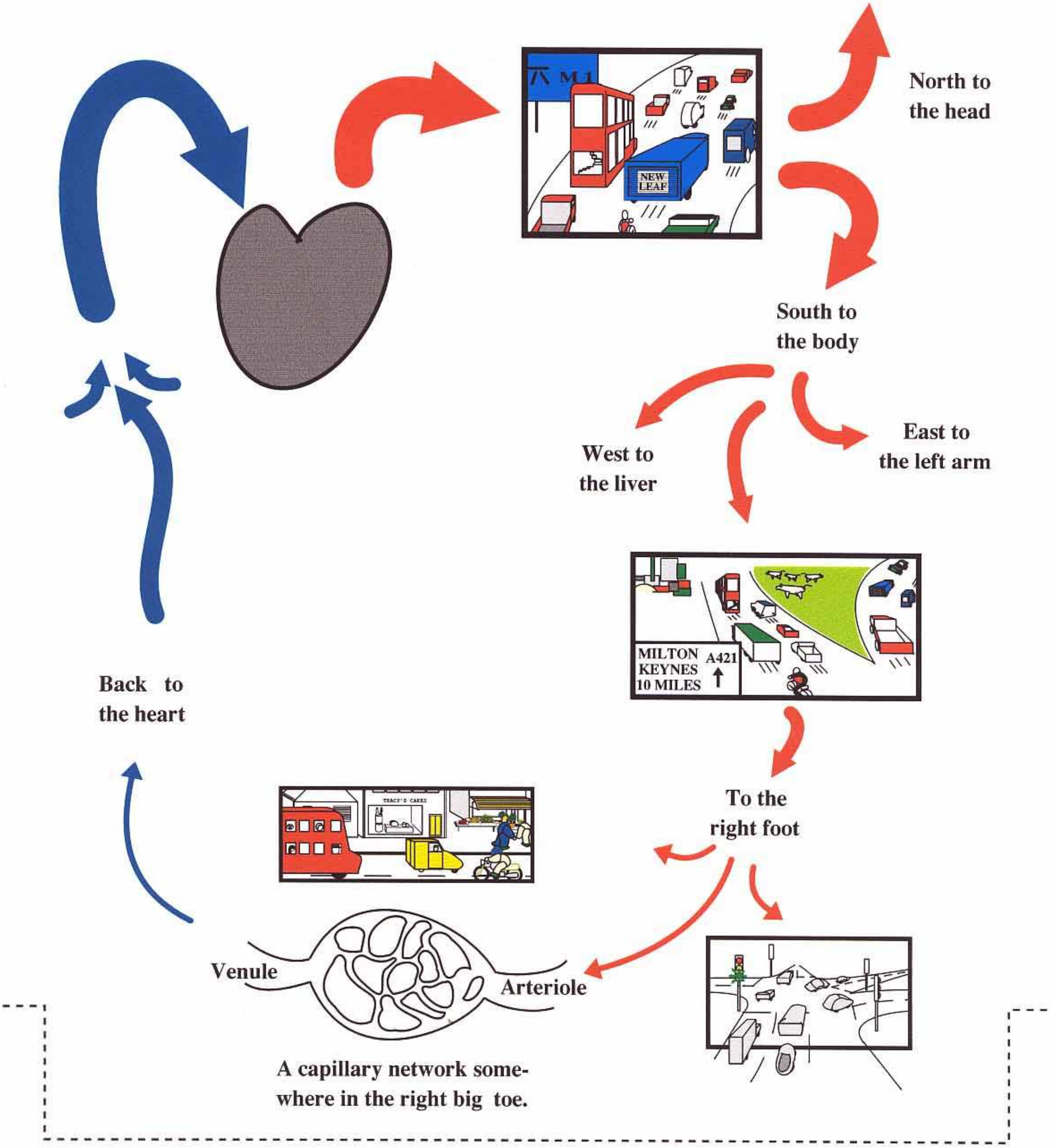


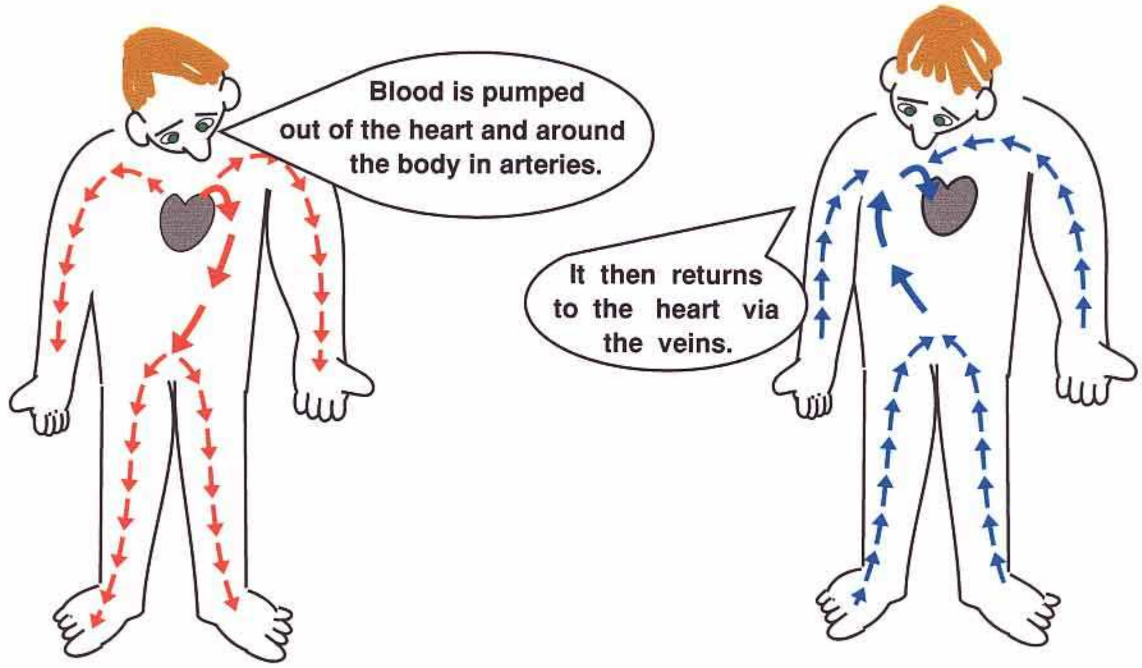
The narrowest artery, called an "arteriole", is linked to the narrowest vein, called a "venule", via a capillary network.

Capillary network



A ROAD MAP OF THE ROUTE BLOOD TAKES TO GET TO A TOE



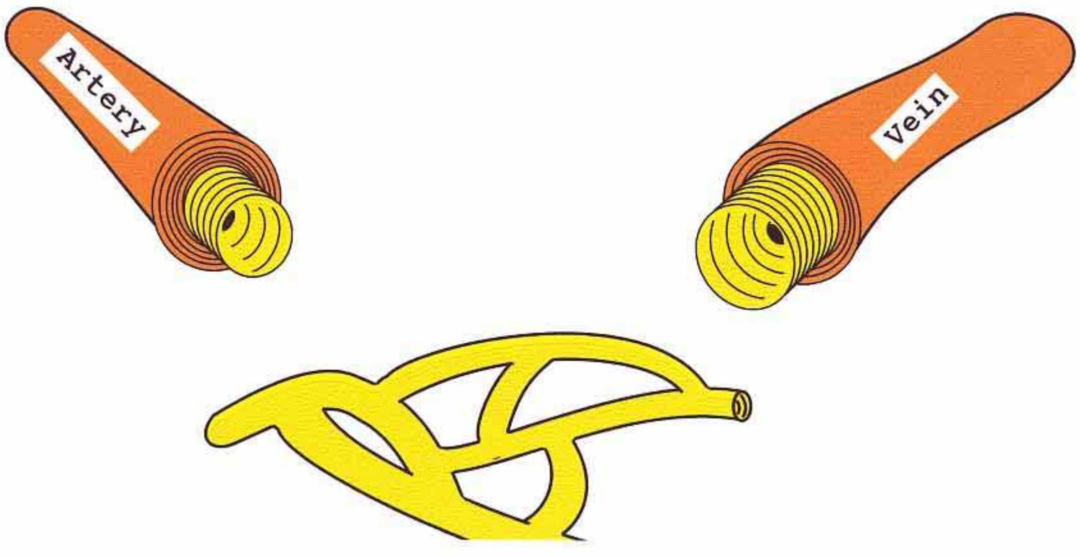


HIGH PRESSURE SYSTEM

LOW PRESSURE SYSTEM

Arteries have thick walls, a narrow bore and are lined with endothelial cells.

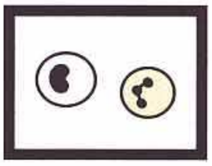
Veins have thin walls, a wider bore and they too are lined by endothelial cells.



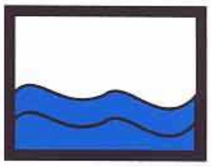
Capillaries are very narrow vessels, with 'wafer thin' walls, made up solely of endothelial cells.

BLOOD

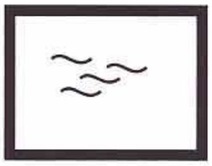
Our blood is red in colour because it contains large numbers of red blood cells. However, it also contains many other vital things such as:-



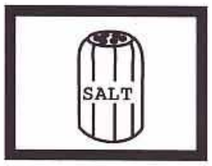
White blood cells



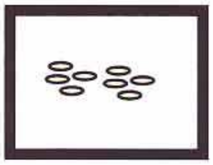
Water



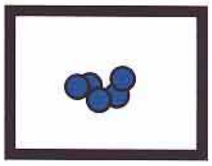
Fibrinogen



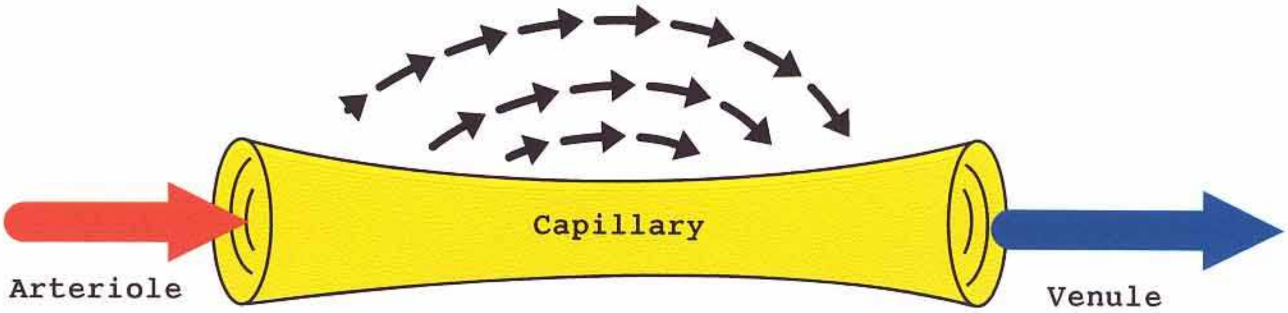
Minerals



Platelets

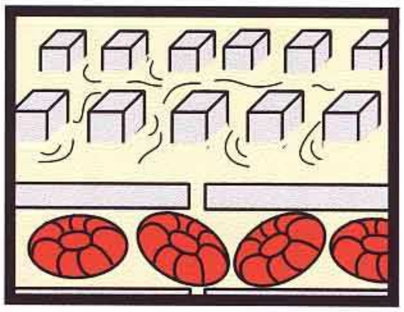


Albumin and globulin

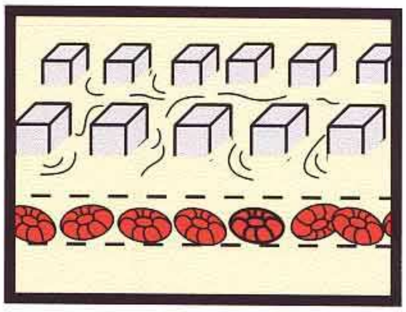


As the capillary is narrower than the arteriole, there is a pressure build up. This forces fluid out of the vessel and into the tissues. Tissue fluid is then drawn back into the venule.

After doing the shopping, the car is left in the street as it is too big to bring indoors!



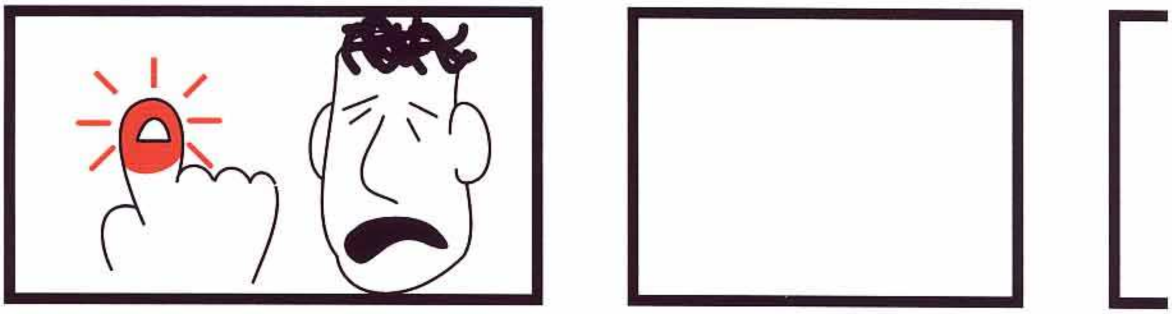
Likewise, red blood cells and other large particles, are too big to pass through the gaps in the capillary walls.



However, water carries small particles through these gaps and into the tissues to bathe the cells.

So if our blood is red, why are we black or white and not red? The answer is simple. The red blood cells which give blood its red colour, are confined to the blood vessels.

INFLAMMATION



The classic signs of an inflammatory response are:- redness, heat, swelling, pain and a loss of function.

SOME OF THE MAIN CAUSES OF INFLAMMATION

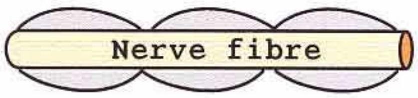
Trauma

Infection

Burns

Fractures

AN INFLAMMATORY RESPONSE



PAIN

Nearby nerves are irritated.

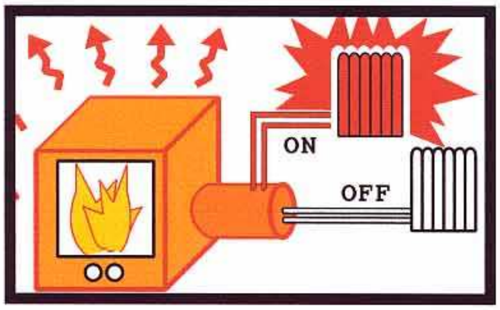
HOT AND RED

Local arterioles dilate to increase the amount of blood entering the affected area.

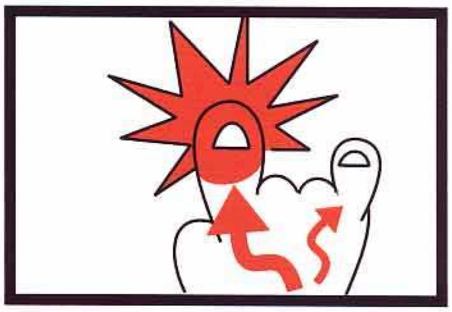
SWELLING

Gaps in the blood vessel walls widen to allow increased fluid and larger particles to escape into the tissues.

DOES A RADIATOR GENERATE HEAT IF IT FEELS WARM?

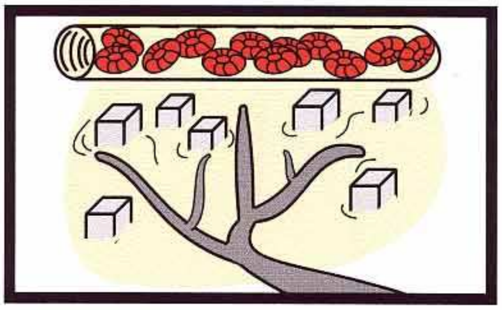


Although a radiator may feel hot, the heat is generated in a boiler.

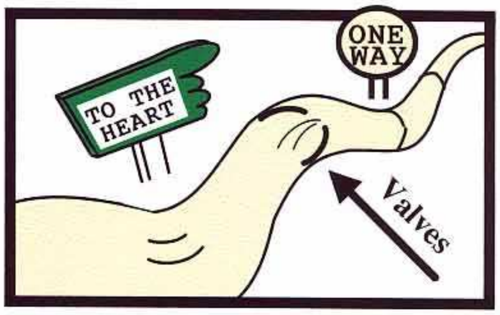


This inflamed finger feels hot, but is the heat generated here?

Again the answer is "no", as the liver acts like a boiler. Local arterioles in the affected part dilate and this then allows more warm blood to enter the affected area.



Some of the tissue fluid bathing the cells (see page 20), drains into lymph vessels.

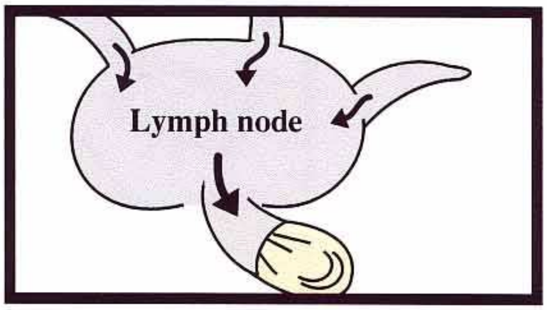


Inside the lymph vessels, valves ensure that the collected fluid (now called "lymph"), only flows one way.

Lymph vessels are found all over the body. They track back to the heart and empty the collected lymph there.

LYMPH NODES

These are found where a number of lymph vessels join together.



Lymph flowing back towards the heart, is filtered as it passes through the lymph nodes.

In Africa, a parasite can block the lymph nodes draining the leg, causing tissue fluid to build up. This condition is known as elephantiasis.

INSIDE A LYMPH NODE

While these macrophages are busy removing debris from the lymph, some B cells appear to be sleeping on the job.

As the lymph passes through the node, any waste material in it is removed.

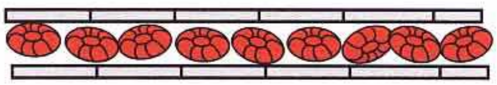
MEET THE B LYMPHOCYTE

He was born and raised in the bone marrow.

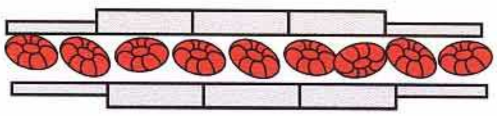
On reaching maturity, the B cell must leave to find a new home.

Carried in the blood, he reaches his new home, a lymph node.

Soon the B cell is eagerly leaving the blood vessel to find out what lies inside.

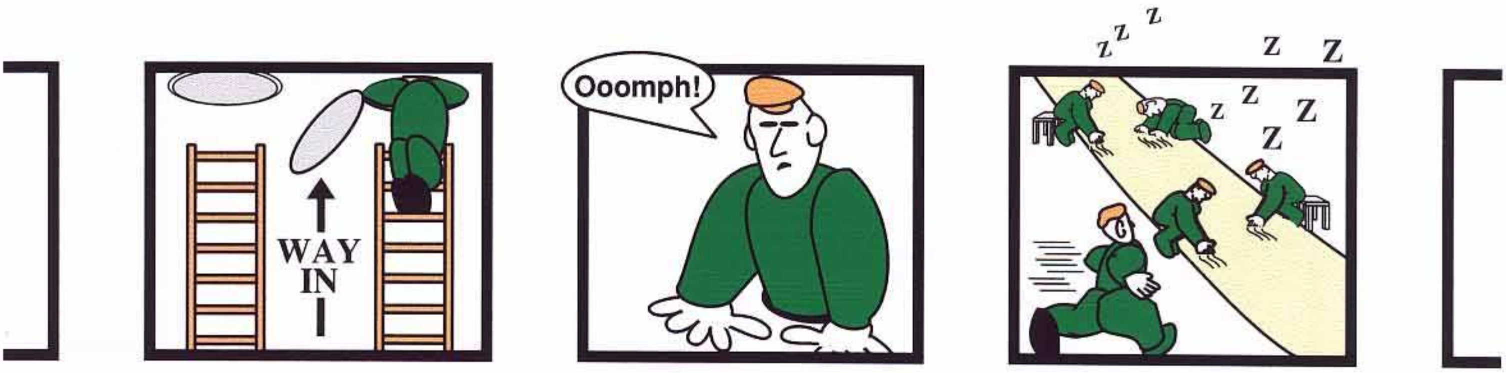


Most blood vessels are lined by thin endothelial cells.

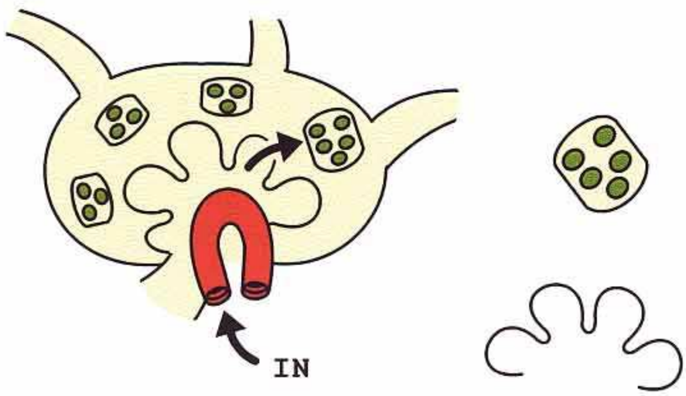


But some veins inside the lymph node are lined with high endothelial venules.

THE YOUNG B LYMPHOCTE'S NEW HOME

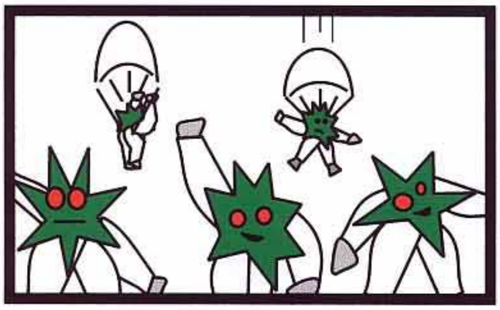


Although it is a tight squeeze getting out of the blood vessel, he is soon joining his brothers in one of the primary follicles.



B cells uses the high endothelial venules to enter a lymph node and then making their way to one of the primary follicles.

POOR PIERCE MYSKIN GETS THE POINT

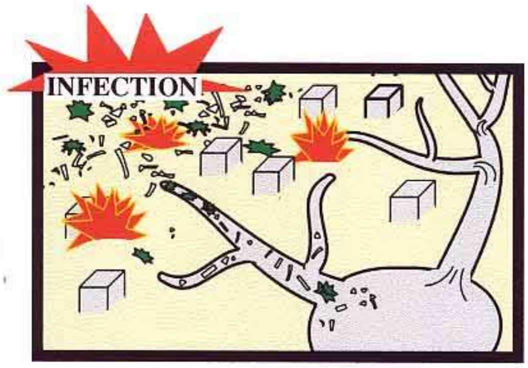


These microbes see the opening and enter the cut to infect his foot.

Alerted to the danger, neutrophils are quick to appear on the scene.

Neutrophils will leave a blood vessel and enter the tissues, if they detect things like traces of bacteria, activated complement or inflammation.

INFECTED DEBRIS GETS WASHED INTO A LYMPH NODE

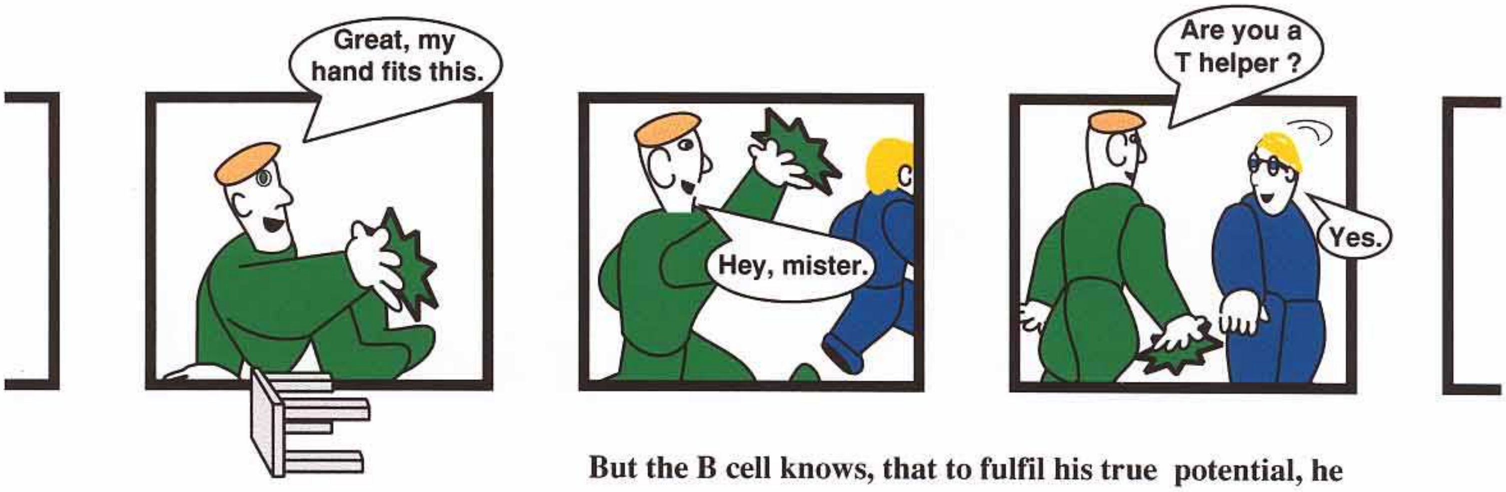


Lymph from the infection is soon draining into this lymph node.

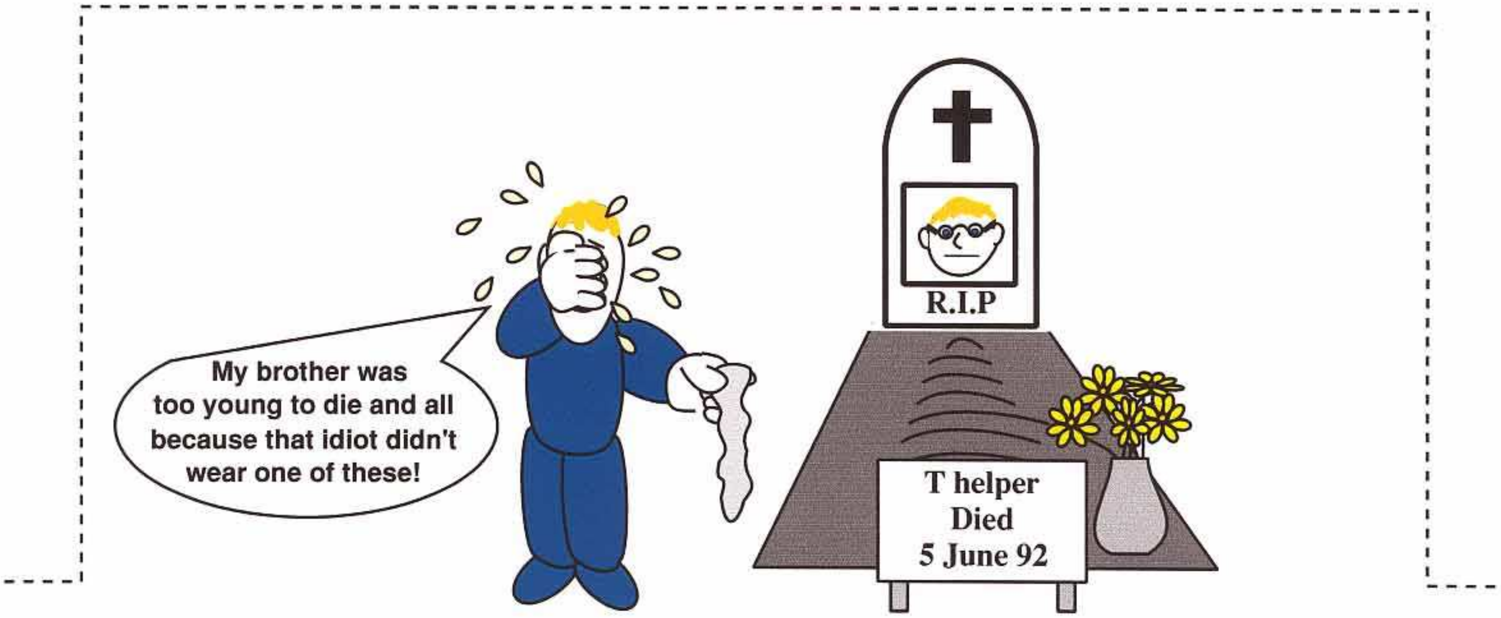
One of the B cell's suddenly 'grabs' a passing microbe.

Unlike the macrophages, each B cell has a unique fixed 'hand' shape, which greatly limits what it can attach onto.

THE B CELL MEETS T HELPER LYMPHOCYTE



But the B cell knows, that to fulfil his true potential, he now needs that special something from a T helper cell.

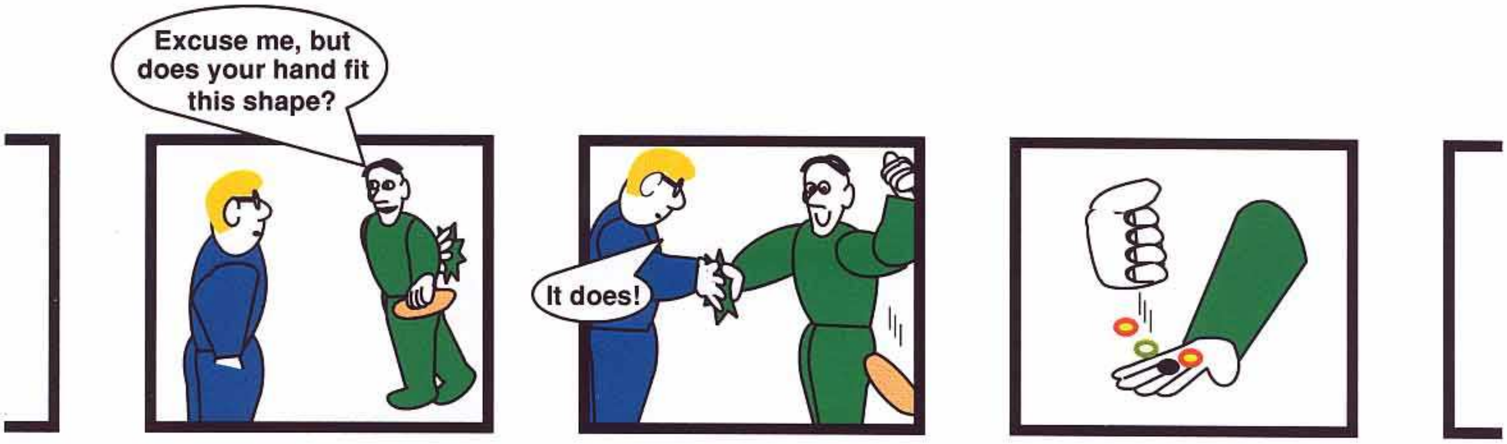


This is the immune cell which the AIDS virus infects and destroys.

THE B CELL IS LET DOWN

Like the B cell, each T helper has a unique fixed 'hand' shape. This greatly limits what he too, is able to attach onto.

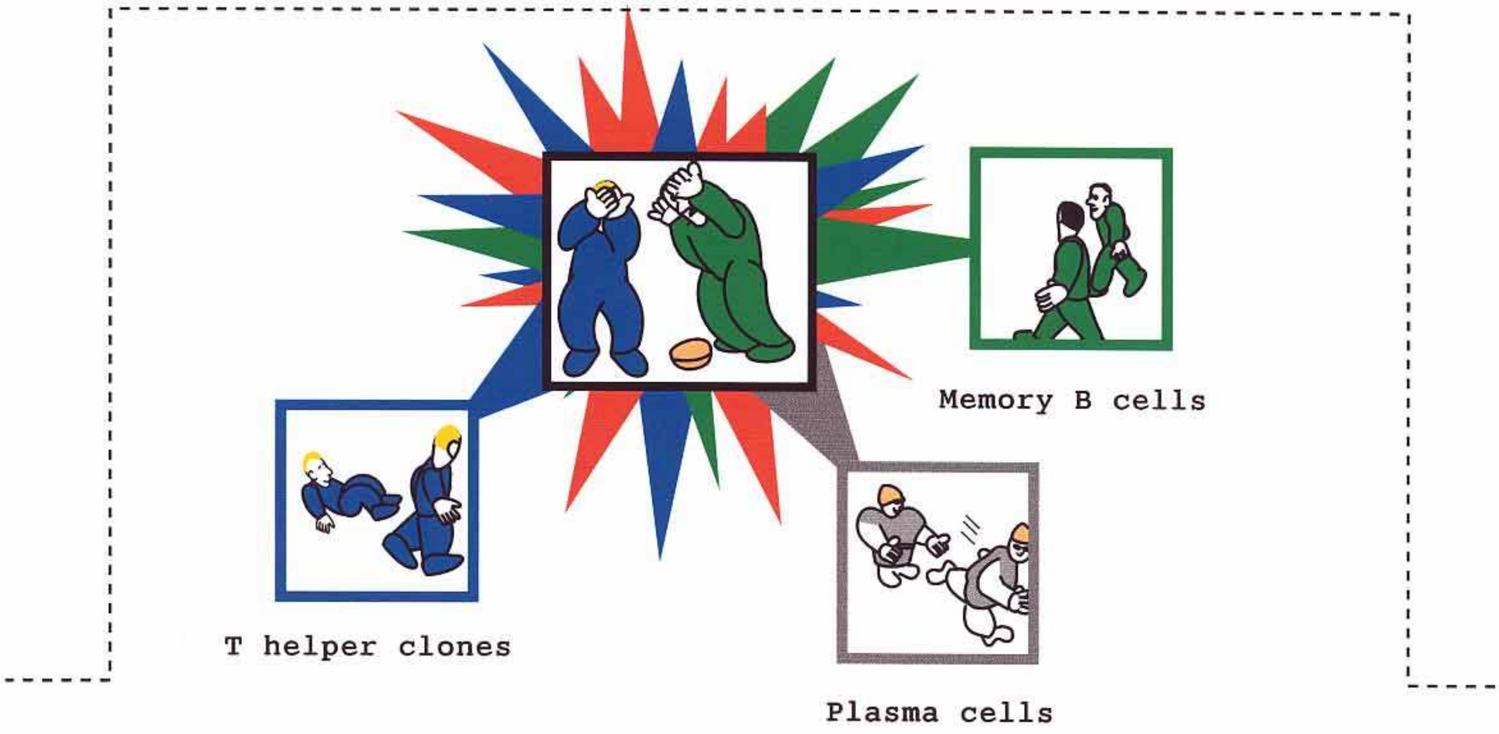
ANOTHER T HELPER ENTERS THE LYMPH NODE



The B cell now meets another T helper cell.

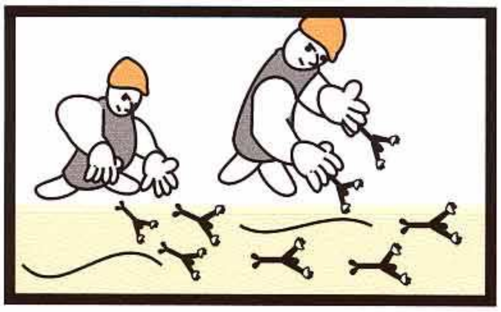
To his great delight, this T helper's 'hand' fits!!

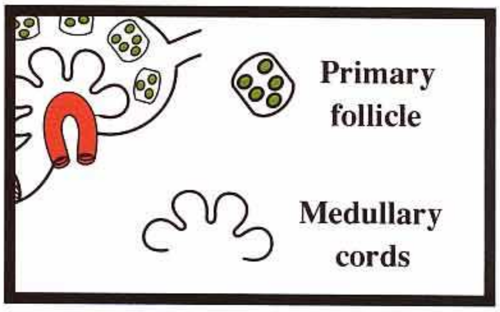
He then gives the B cell something interesting.



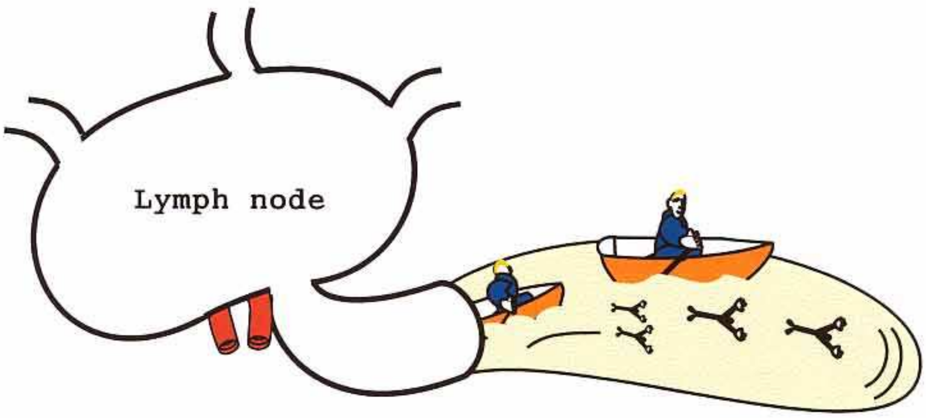
If the T helper's 'hand' fits, it releases factors which affect both cells. The T helper clones itself and the B cell changes into plasma cells and memory B cells.

AS THE DUST SETTLES



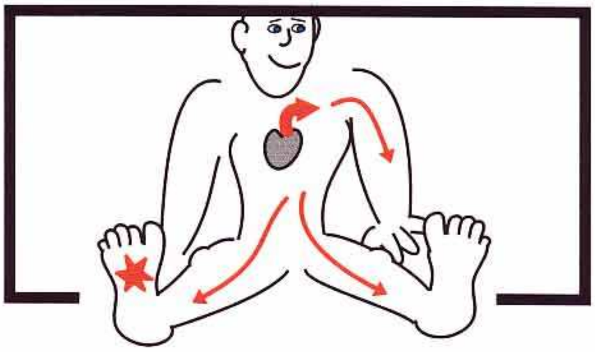


Leaving their primary follicle, the plasma cells will go to the medullary cords. Here, they will each start to release large quantities of antibodies.

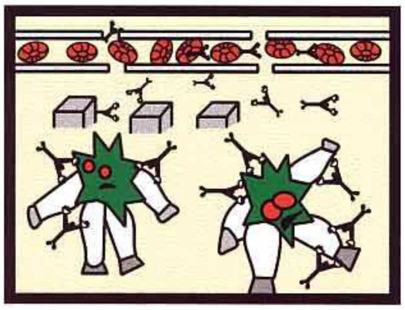


`Lymph flowing out of the node on its journey back to the heart, now contains antibodies and T helper cells.`

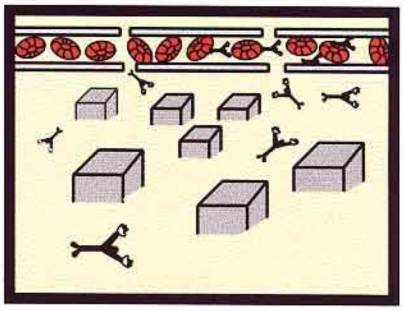
PIERCE MYSKIN'S ANTIBODIES DO THE TRICK



From the heart, the antibodies are carried around his body in the blood.



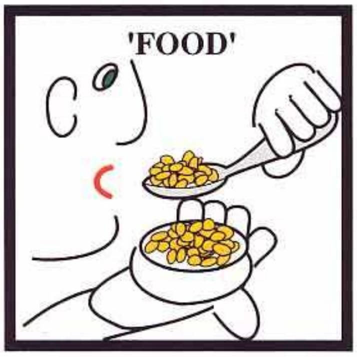
Entering the infected part of the foot, the antibodies apprehend the microbes.



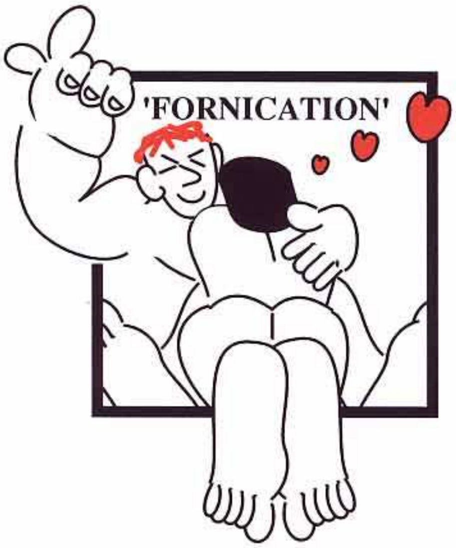
They also enter the uninfected foot, but here there's nothing to attach onto.

Antibodies, unlike red blood cells, are small enough to pass out through the small gaps in the capillary walls and into the tissues.

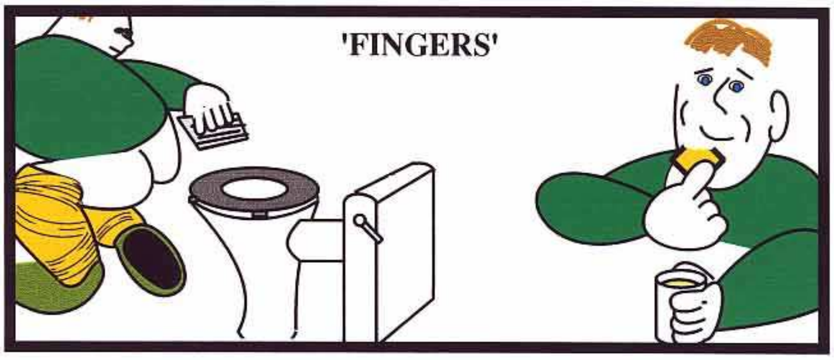
INFECTION AND THE 5 DEADLY F's



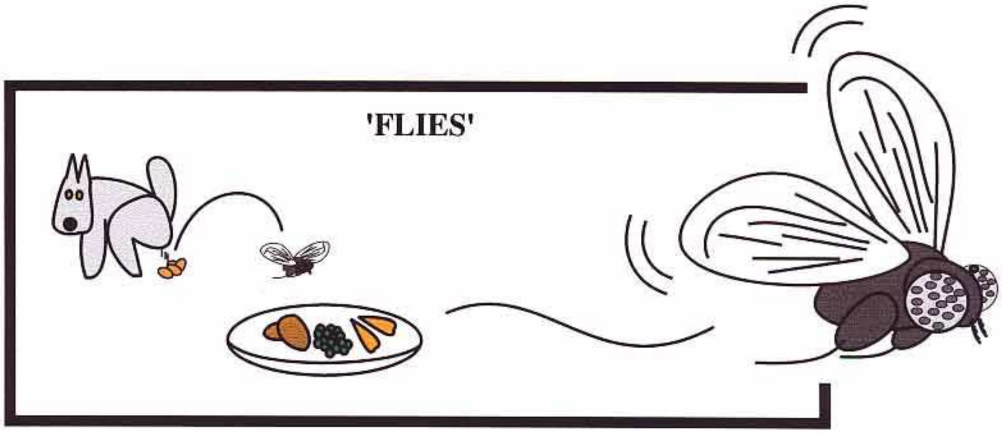
Eating or inhaling any contaminated material.



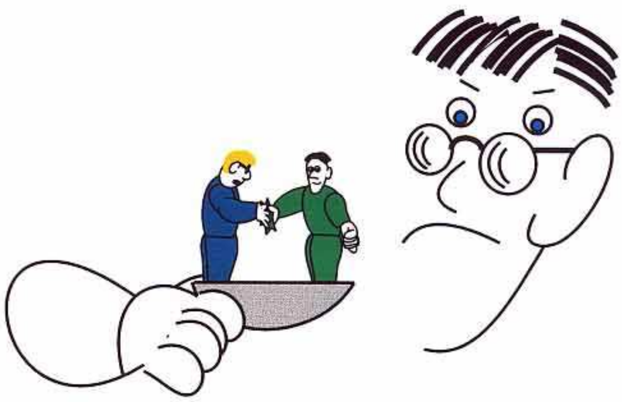
Touching an infected inanimate object (ie a tap).



Just think where your fingers might have been and where they may now be going!!



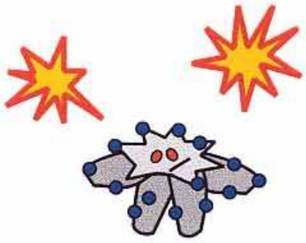
This method of transferring germs, involves living things (ie flies, dogs etc), physically carrying microbes from A to B.



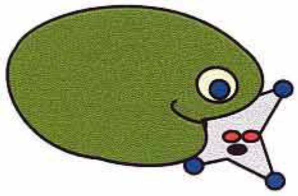
In the laboritory, scientists find it very difficult to get T helper cells to stimulate B cells into releasing antibodies. To see what is missing, turn to page 289.

MORE FACTS ABOUT COMPLEMENT

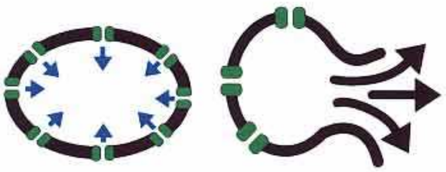
(see page 5)



When complement comes into contact with a microbe, it 'sticks' to its surface and causes inflammation.



The pieces of complement 'sticking' to the microbe, make it much easier for an immune cell, to now 'eat' the blighter (see page 268).

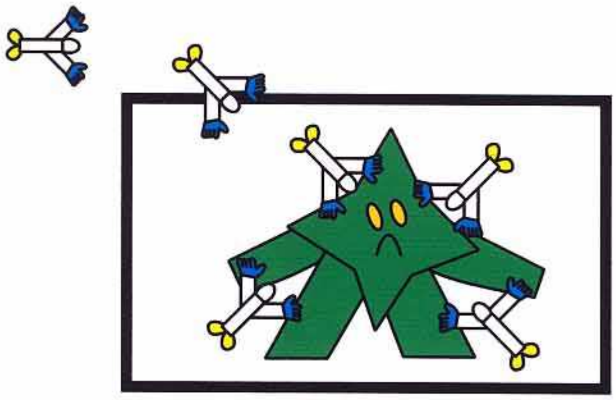


Complement also forms pores in the surface of the microbe. These allow water to flow into it, so that the microbe swells and then bursts.

CHAPTER TWO

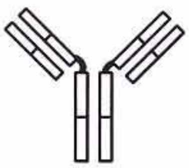
ANTIBODIES

ANTIBODIES ARE USED TO APPREHEND INVADING MICROBES

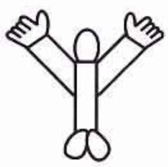


Easy reading

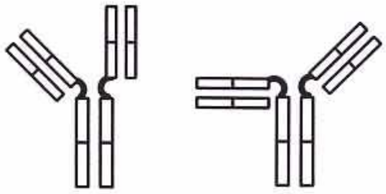
Technical information



Antibodies are 4 chains of molecules linked together.

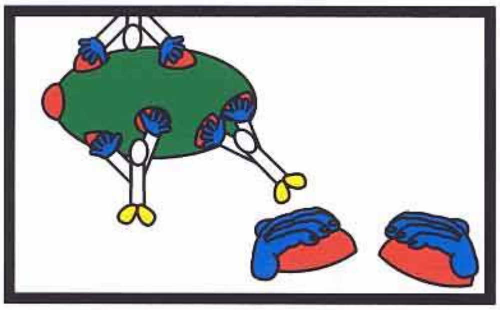


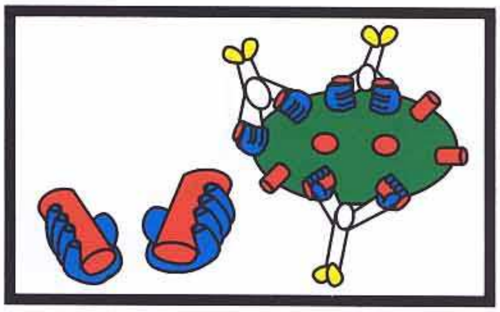
These function as 'hands', 'arms', a 'body' and 'feet'.



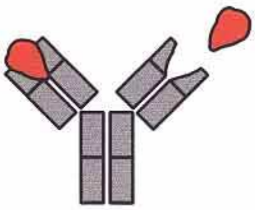
The 'arms' are hinged so that they can move.

'HANDS'



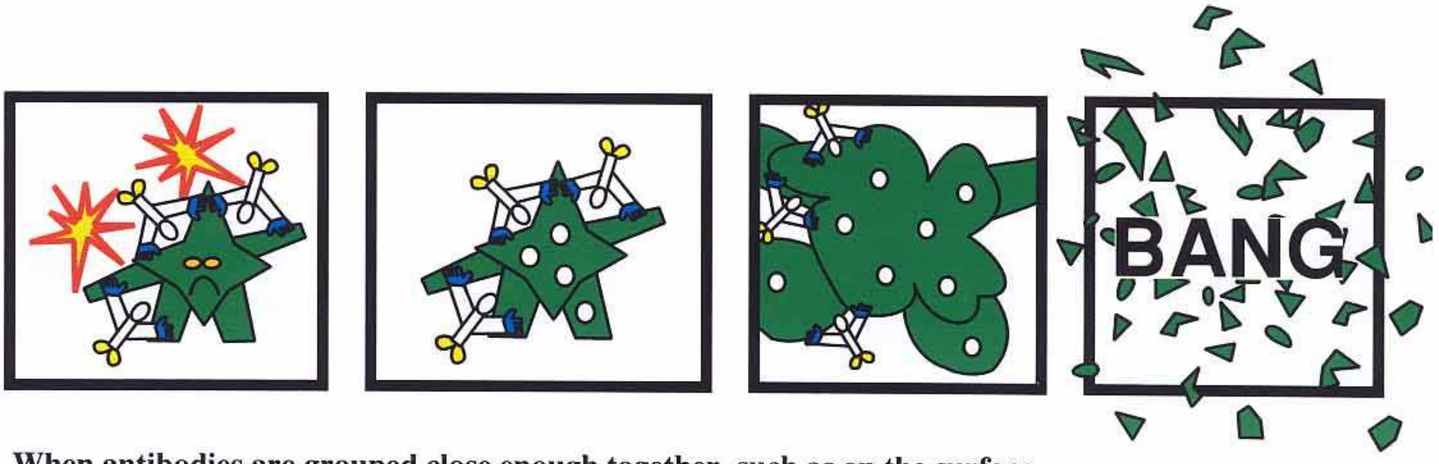


Both these sets of antibodies are identical, apart from the shape of their 'hands'.

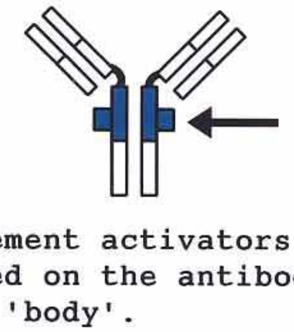


```
As an antibody's 'hand' shape is fixed,
to apprehend a microbe, the 'hands' must
fit snugly around and over the target.
```

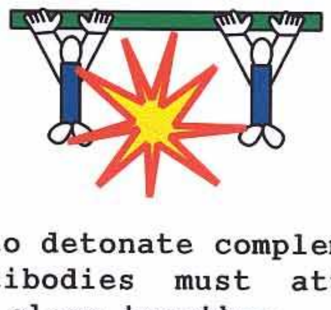
THE 'UPPER BODY'



When antibodies are grouped close enough together, such as on the surface of a microbe, they will activate complement and blow it to pieces!!

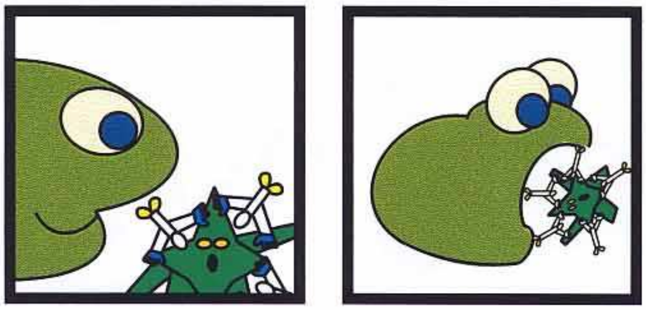


Complement activators are located on the antibody's upper 'body'.

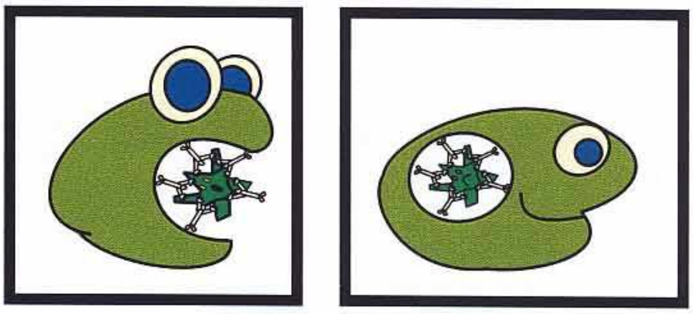


But to detonate complement, 2 antibodies must attach very close together.

THE 'FEET' / LOWER BODY

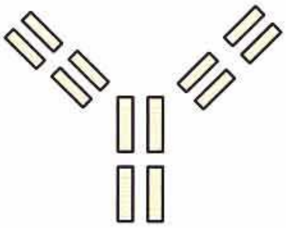


Macrophages and neutrophils, use surface receptors to attach onto the 'feet' of those antibodies coating the surface of a microbe.

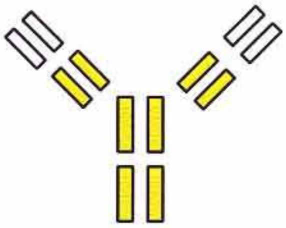


As they attach onto more and more antibodies, so the microbe is drawn inside the immune cell (like a zip being fastened), until it is totally enclosed.

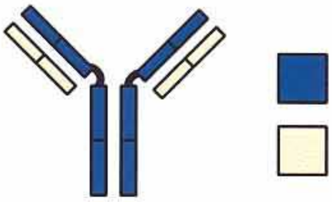
The 'feet' (end section) of the antibody are used by immune cells, to attach (opsonize) onto foreign material.



Antibodies are made up of a number of domains or regions.

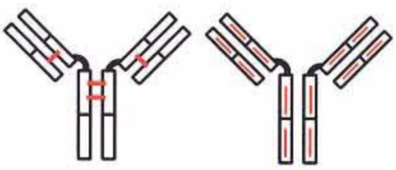


The constant domains (shown in yellow) are of a universal design.

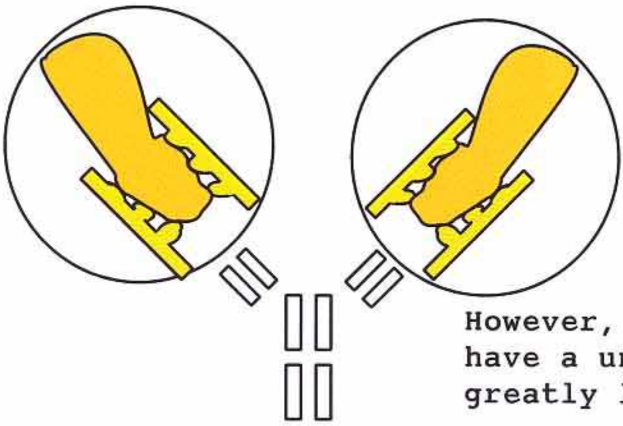


2 heavy (long) molecular chains.

2 light (short) molecular chains.

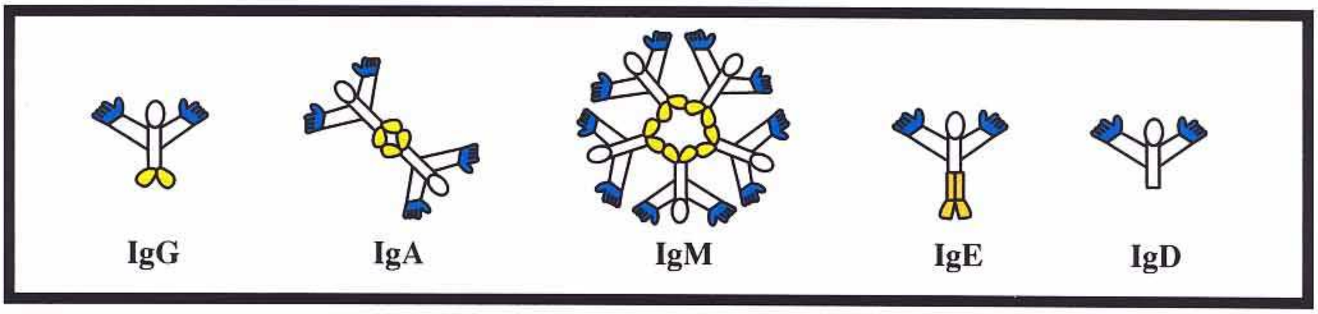


Strong disulphide bonds (shown in red), maintain the antibody's structure.

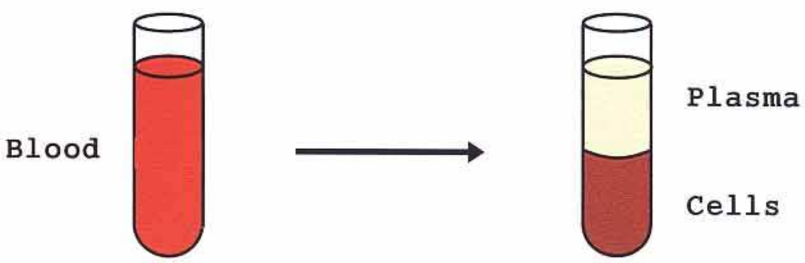


However, the variable domains ('hands') have a unique internal structure, which greatly limits what can be 'held'.

THE CLASS OF 5

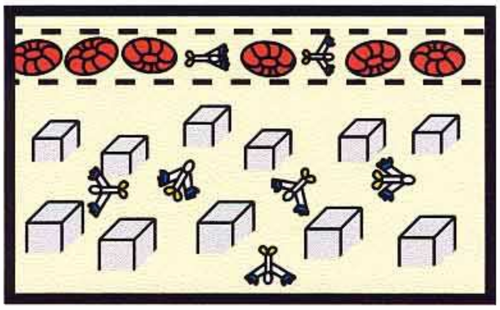


There are actually 5 classes of antibodies:- G, A, M, E and D.



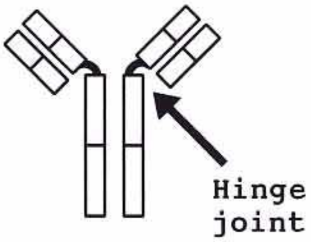
Fresh blood can be separated out into cells and plasma. Antibodies, a group of globular proteins found in the plasma, may be called "immunoglobulins" or Ig for short.

<u>**IgG**</u>

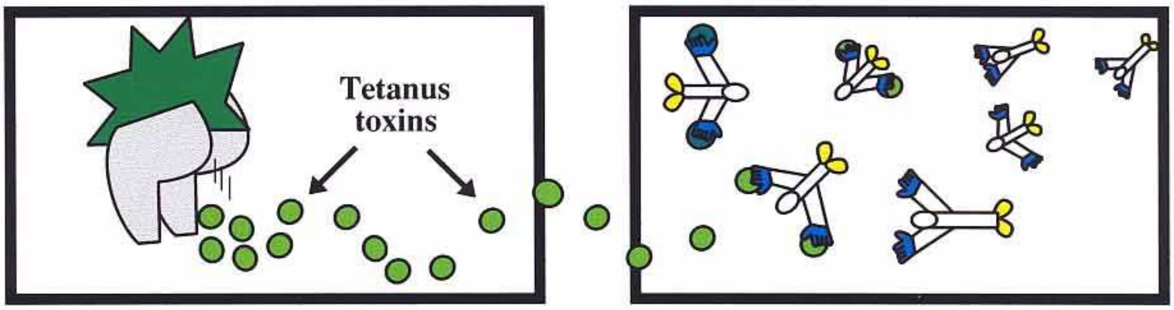


IgG are small enough to pass out of the blood and into the tissues.

A mother's IgG can pass through the placenta and into her foetus.



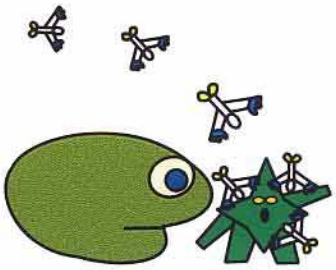
Newborn babies start making IgG after about 4 months. In the adult, it is the commonest antibody in the plasma.



Some bacteria (eg Clostridium tetani) produce toxic waste called "exotoxins".

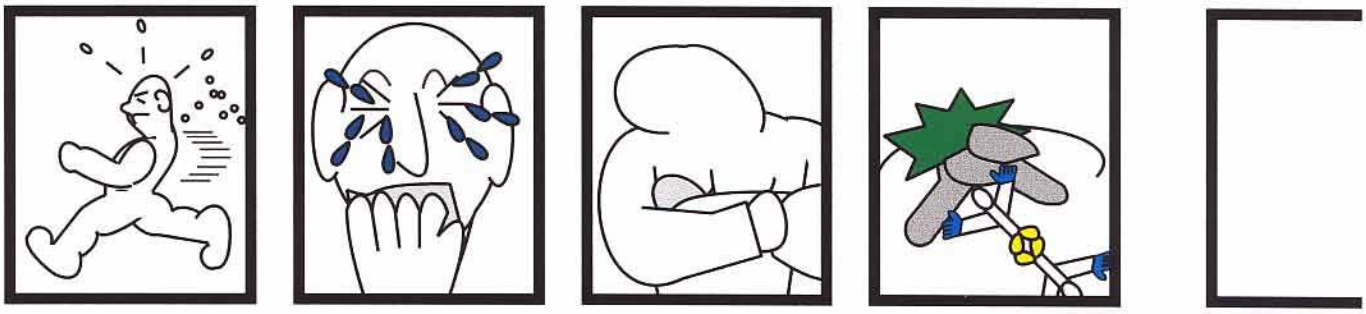
IgG are very effective at 'grabbing' these before they can do any harm.

2 IgG attached very close together, will activate complement.

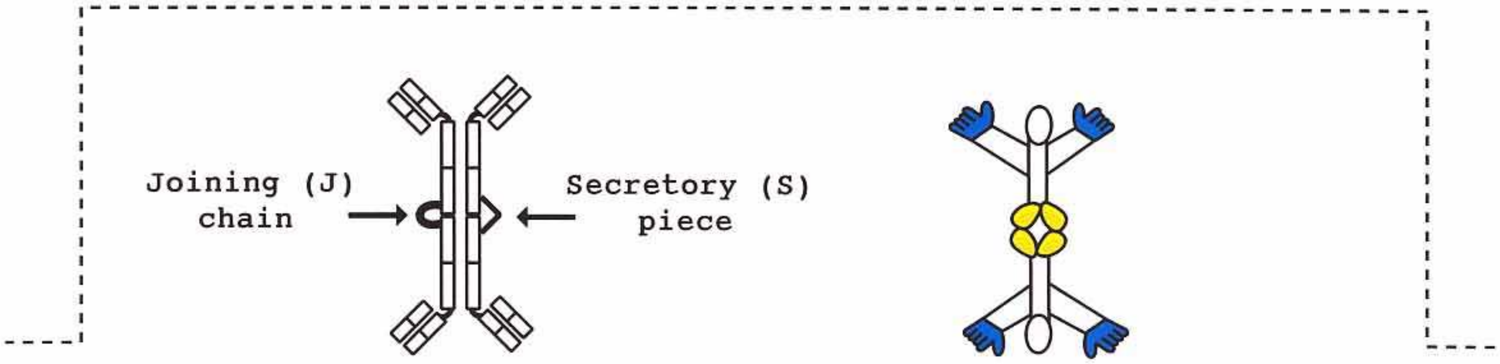


When attached onto anything, IgG 'feet' help immune cells to 'eat' foreign matter.

IgA



IgA antibodies are not found in the blood. They are secreted onto the surface of the body, in things such as:- sweat, tears, a mother's breast milk and mucus.



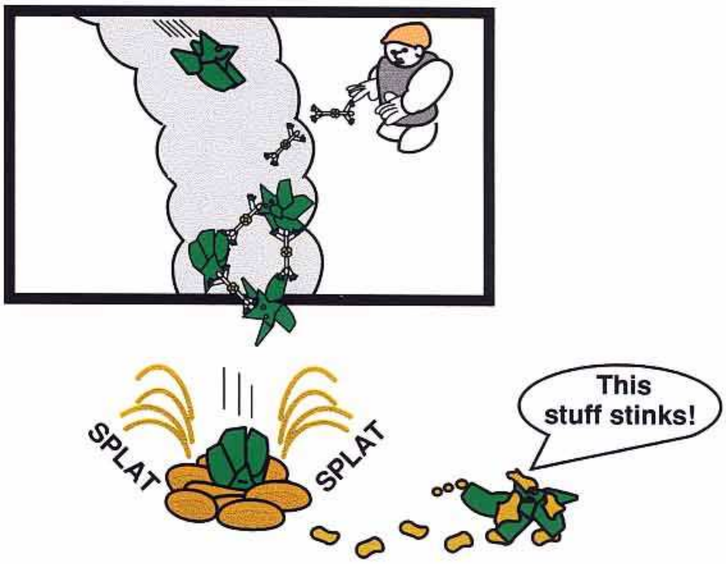
This class of antibody has 4 identically shaped 'hands', but is unable to activate complement.

HE DOESN'T REALISE HIS MEAL IS CONTAMINATED

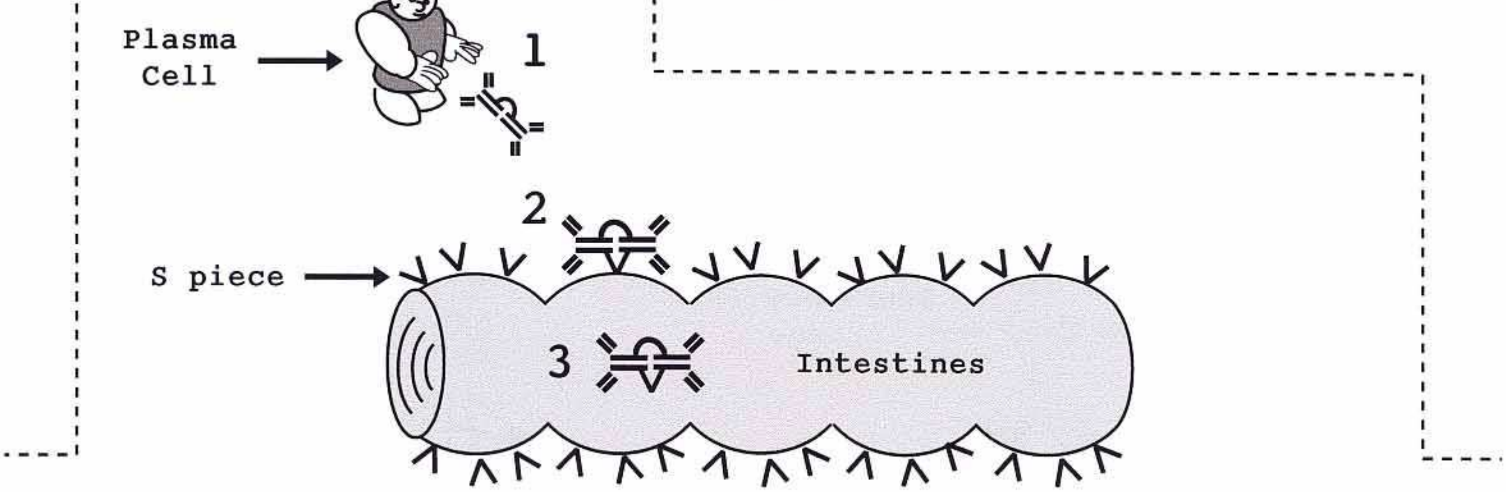
INSIDE HIS INTESTINE (INFECTION)

INSIDE HIS INTESTINE (IMMUNITY)

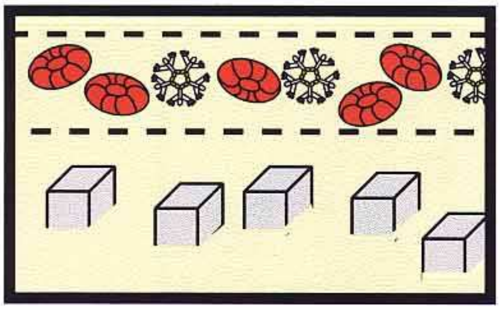
Microbes in his food, attach and penetrate the gut wall.



IgA 'grab' the microbes. This stops them attaching onto the gut wall and they are excreted in faeces.



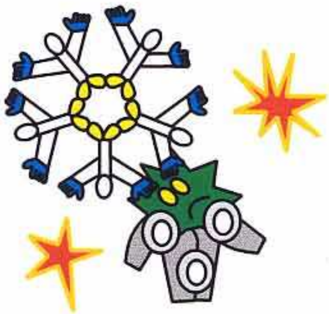
1. Plasma cells release IgA antibodies.
2. The IgA then attaches onto an S piece, lining the 'outer' gut wall.
3. The S piece then transports the IgA through and into the intestines.



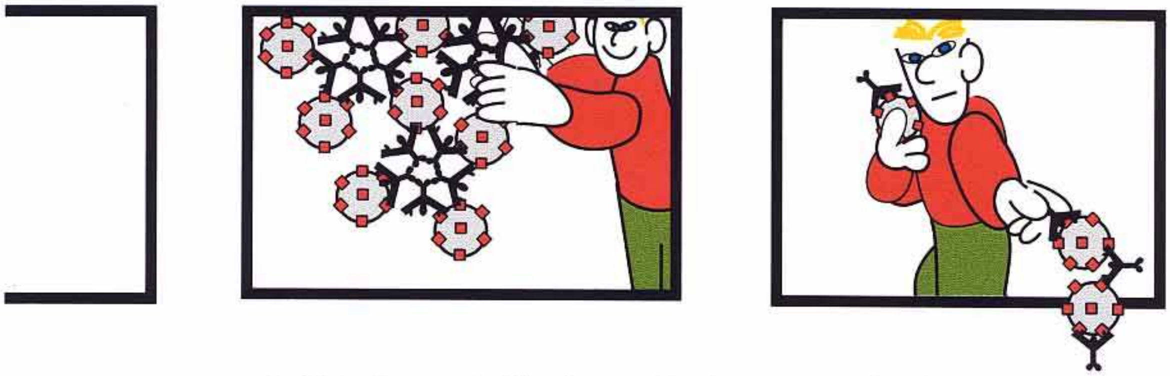
IgM antibodies are only found in the blood. They are too big to pass through the blood vessel walls and into the tissues.

An unborn foetus will start to make this class of antibody at around 5 months gestation.

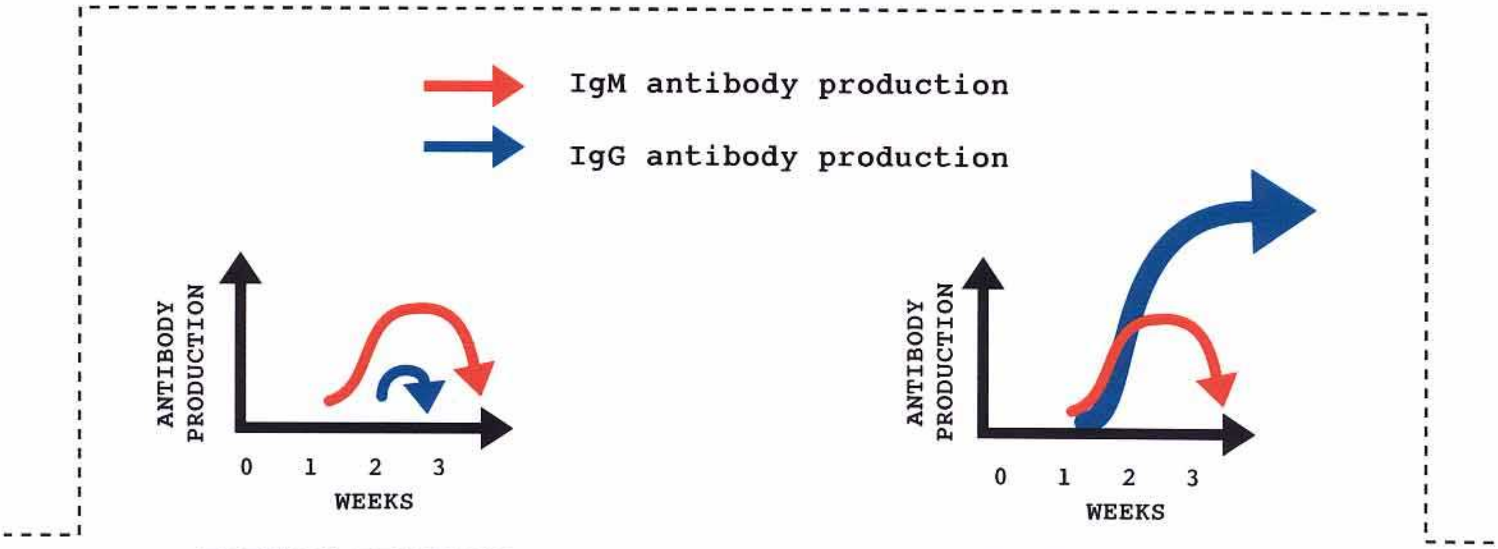
- Joining (J) chain
- Disulphide bonds
- * No hinge joints
- * 10 identical 'hands'



It only takes one IgM to 'grab' something for it to activate complement.



IgM is the most effective antibody at agglutinating ('clumping') foreign material together. Much can be eliminated in one go!!



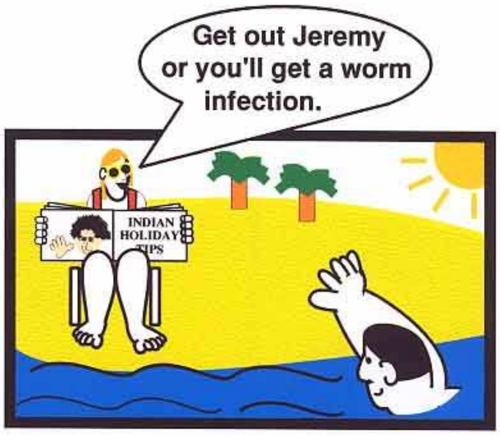
PRIMARY RESPONSE

When foreign matter appears for the first time, mostly IgM antibodies are released.

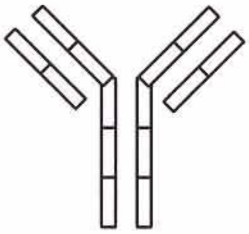
SECONDARY RESPONSE

But if the same thing reappears:-
IgM response remains unaltered.
IgG response greatly increases.

Unfortunately, IgE antibodies can trigger violent, allergic reactions.



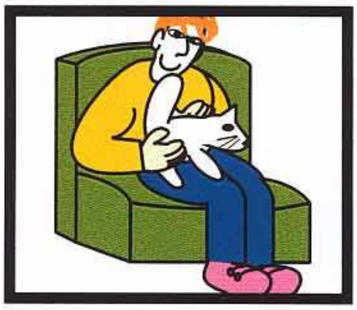
However, these antibodies do help to eliminate parasitic infections.



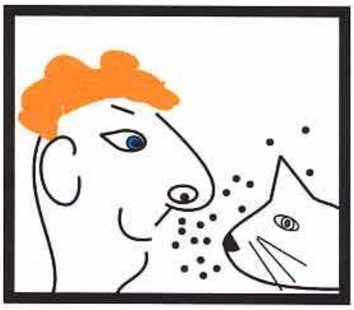
The IgE antibody does not have any hinge joints, so their 'arms' cannot move.

However, they have an extra domain, ('special boots'!).

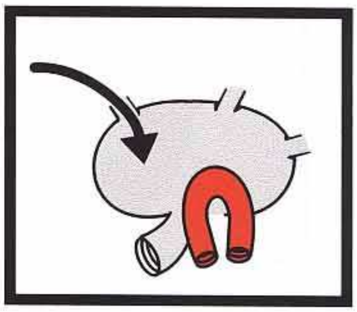
ALLERGY



Paul is stoking a cat.

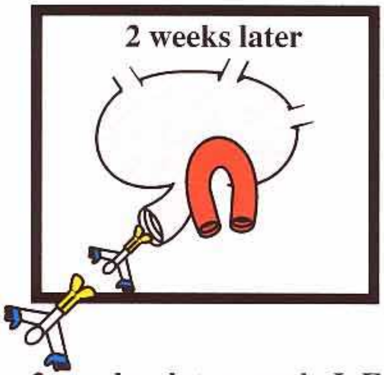


Particles from the cat are soon being inhailed.

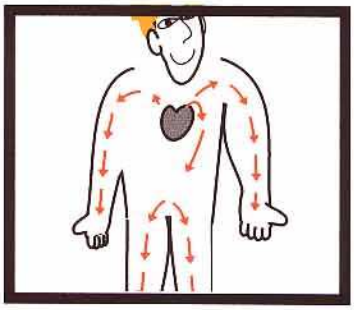


Some of these end up entering a lymph node.

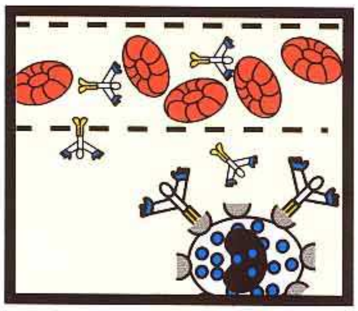
THE CAT IS LONG GONE!



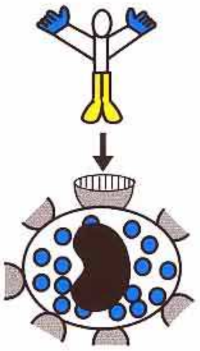
2 weeks later and IgE antibodies start to appear from the lymph node.



Soon they are travelling all around his body and into the tissues.

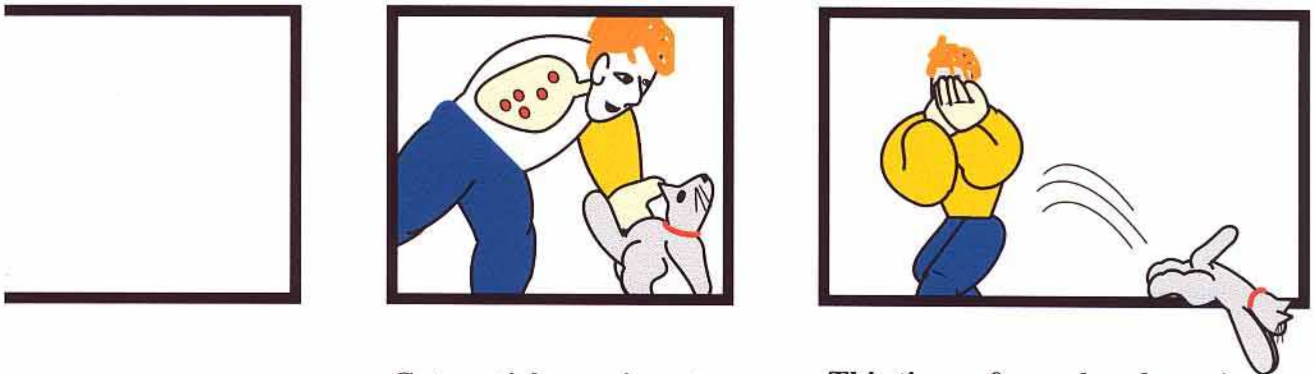


In the tissues, the anti-cat IgE attach onto mast cells using their 'special boots'.



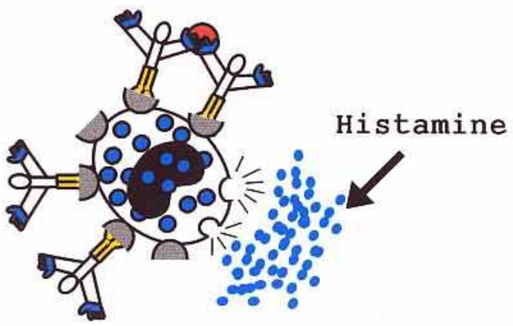
A mast cell has a bean-shaped nucleus, granules which contain histamine and their surface is coated in IgE 'boot' receptors.

WEEKS LATER, PAUL MEETS ANOTHER CAT

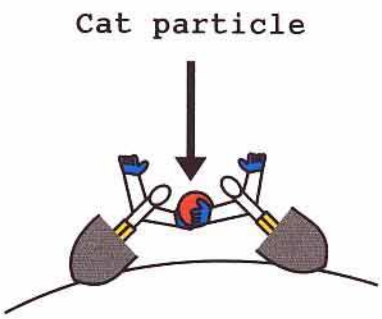


Cat particles again enter his lungs.

This time, after only a few minutes, Paul can hardly breathe.



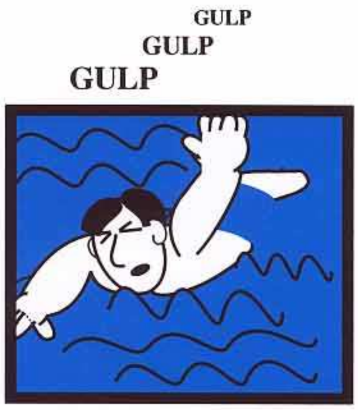
Mast cells close to the lungs, were triggered into releasing histamine, which initiated a violent inflammatory response.



To activate a mast cell, adjoining IgE lining a mast cell (with the same shaped 'hands'), must attach onto the same object (allergen).

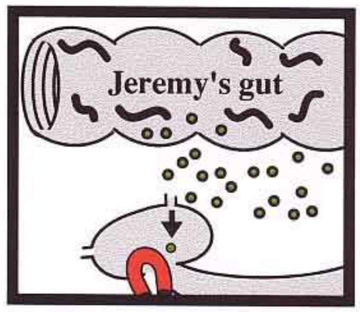
The immune systems of people who experience allergic reactions, for an unknown reason, have released IgE and not IgG antibodies against a particular substance (ie dust mites).

ERADICATING PARASITIC INFECTIONS

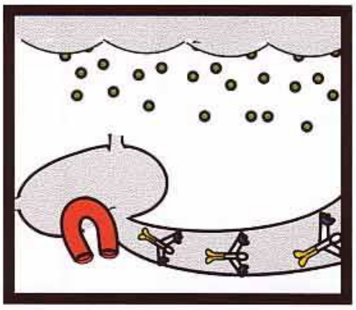


Jeremy swallows some contaminated water.

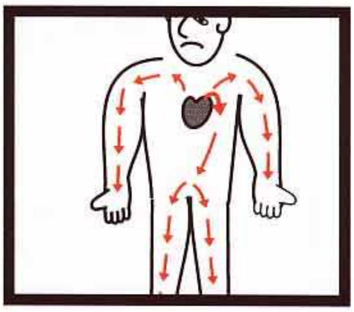
Not long after, worms begin to replicate inside him.



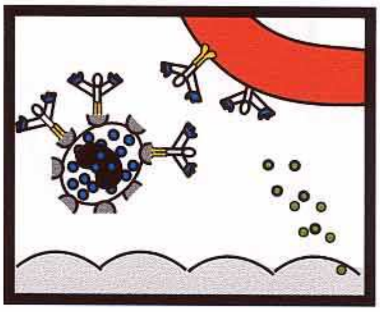
Worm particles reach a nearby lymph node.



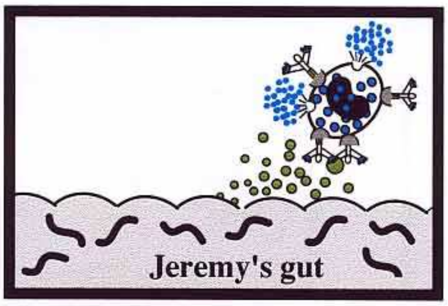
2 weeks later, anti-worm IgE start to appear from the lymph node.



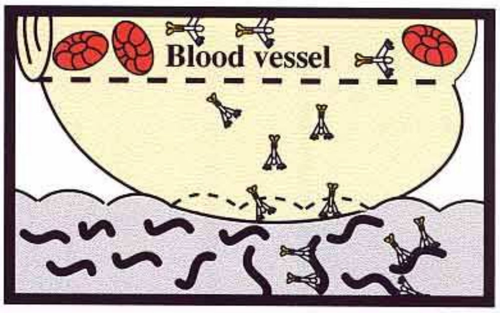
On entering his heart, the IgE are pumped around his body.



Soon the mast cells close to the affected part of the gut, are coated with these IgE.



So it is not long before a mast cell is triggered into releasing its stored histamine.



The resulting inflammation allows plasma, carrying anti - worm IgE, to pass from this blood vessel into the gut and attach onto the worms.

Inflammation is covered in greater detail in chapter 15.

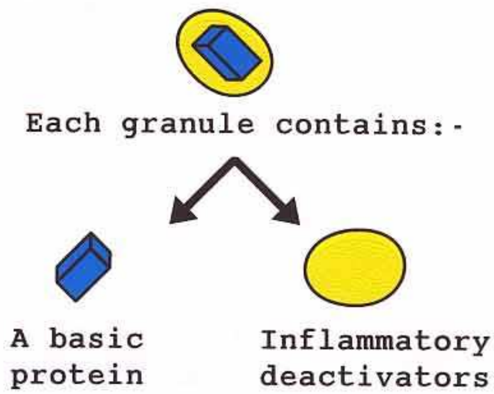
MEET MR EOSINOPHIL

Mr Eosinophil, one of our white blood cells detects trouble.

So he goes to investigate.

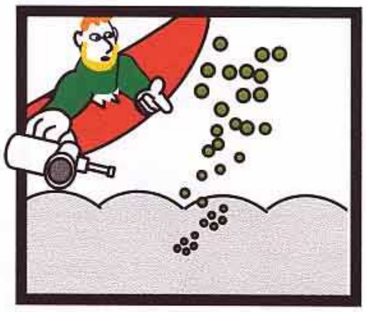
Soon he is squeezing out of the blood vessel.

The eosinophil has a bean-shaped nucleus and unusual granules.

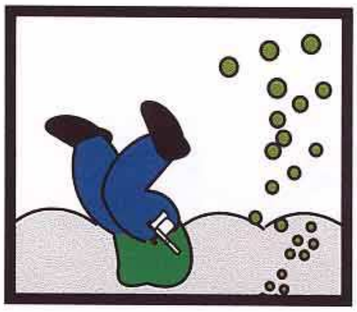


MR EOSINOPHIL EMERGES INTO A DENSE INFLAMMATORY FOG

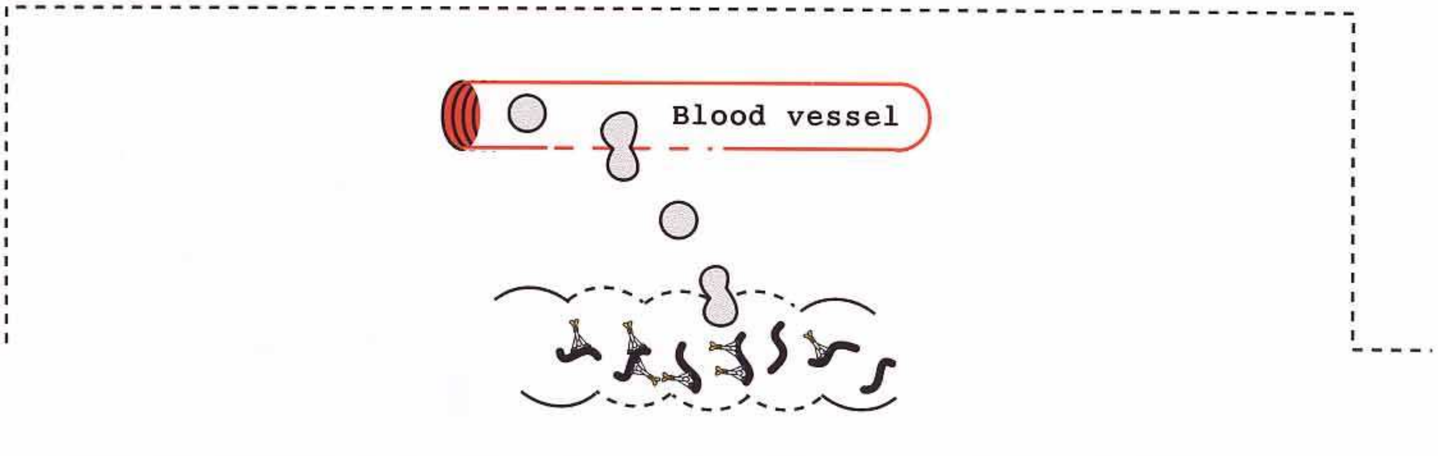
He emerges into dense inflammation and has to use his 'deactivator gun'.



It was then obvious that something ominous was leaking from the gut.



So he decides to take a closer look.

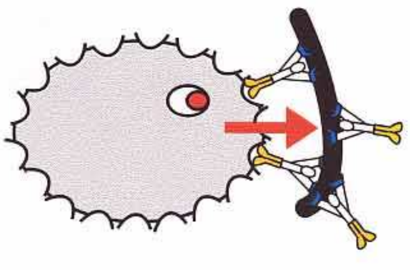


Attracted by factors from the mast cell, the eosinophil leaves the blood vessel, deactivates the histamine and then enters the gut.

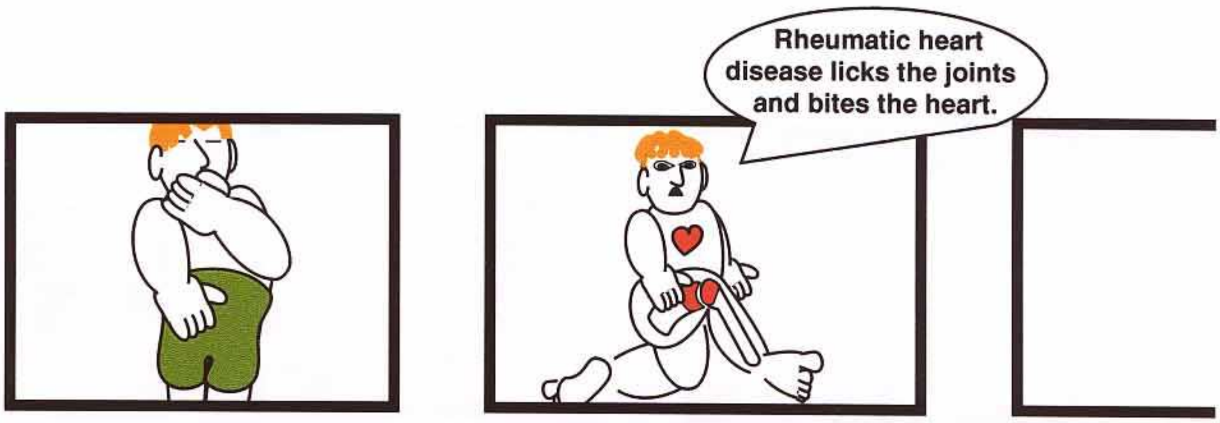
MR EOSINOPHIL DROPS IN

As Mr Eosinophil enters the gut, he 'sees' the problem.

Dropping down into the gut, he wades over to the worms. Being coated in IgE, they are easy to get hold of and killed.



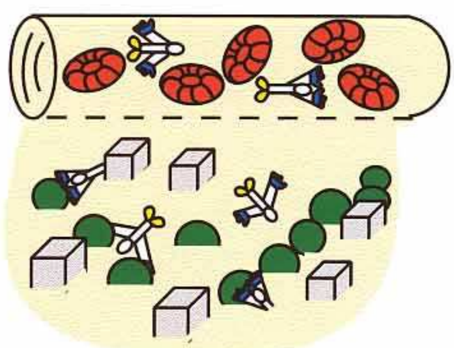
An eosinophil uses its surface IgE 'boot' receptors, to attach onto the parasite coated in IgE, before discharging its killing granules.

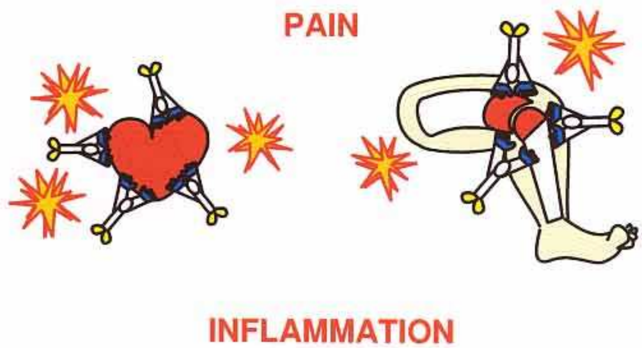


This young adolescent has a nasty cough and sore throat.

2 weeks later, he experiences severe heart and joint pains.

RHEUMATIC HEART DISEASE

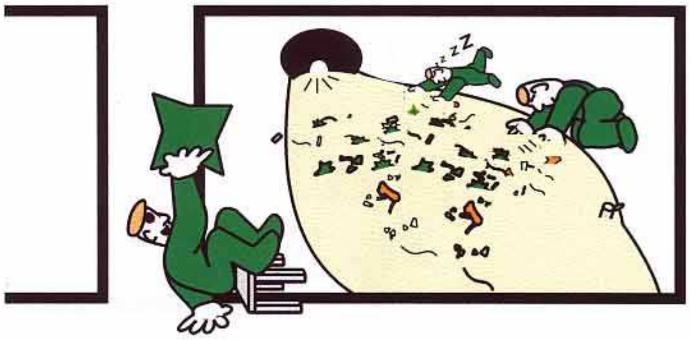




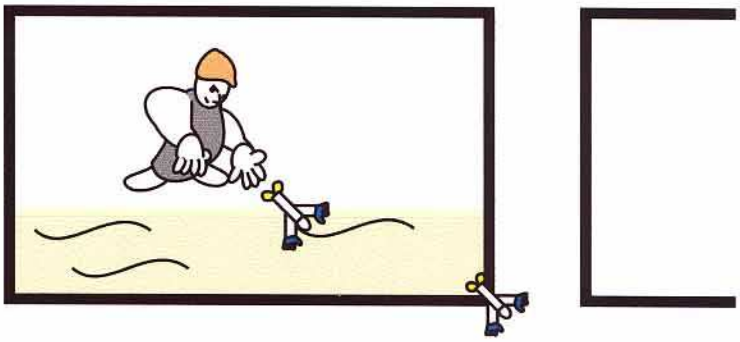
Antibodies arrive in the throat to eliminate the infection, by 'grabbing' the bacteria.

Unfortunately for this young boy, their 'hands' also fit his joints and heart muscle, which causes complement to be activated.

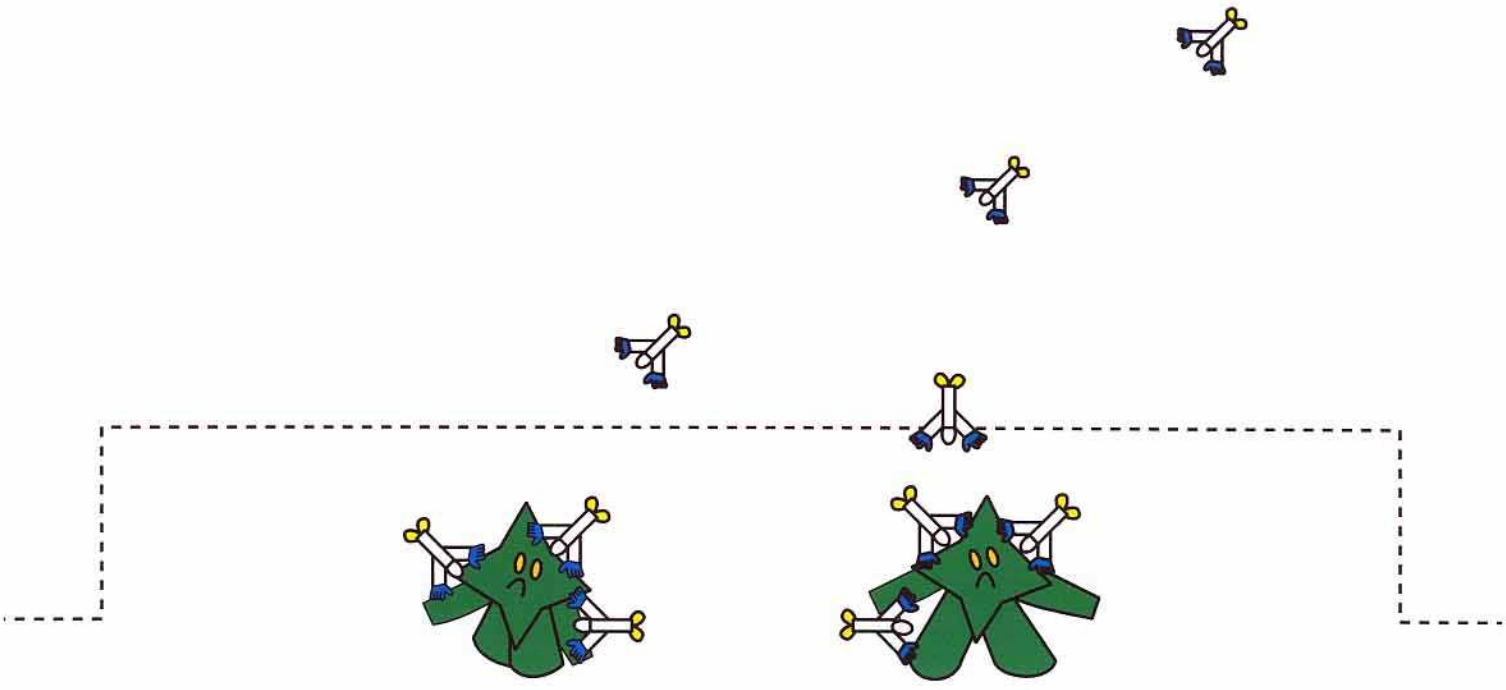
LUCKILY OUR ANTIBODIES RARELY HARM US



Unlike the other B cells, this B cell's 'hands', fits a passing piece of microbe.

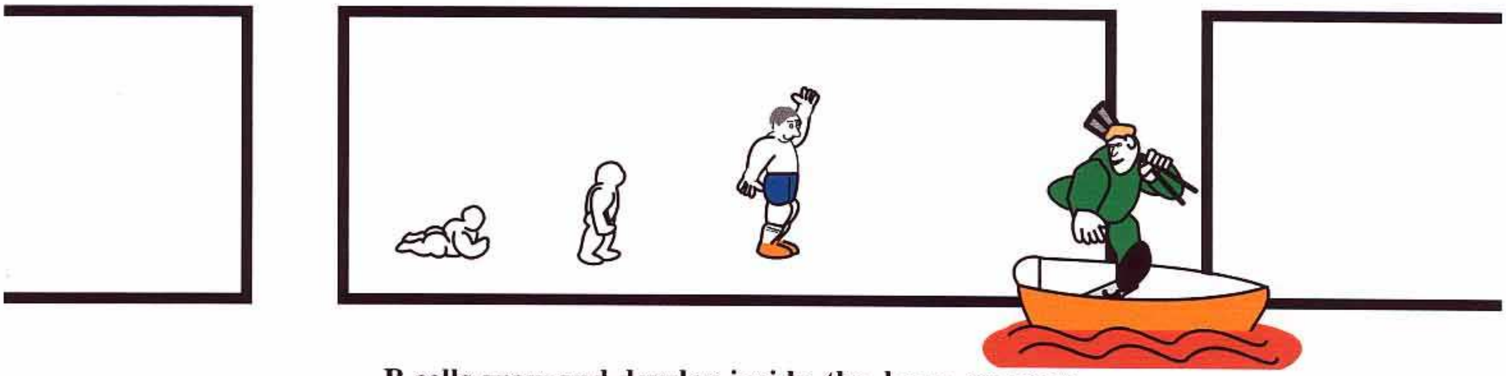


Transforming into a plasma cell, it releases antibodies which have identically shaped 'hands' to its own.

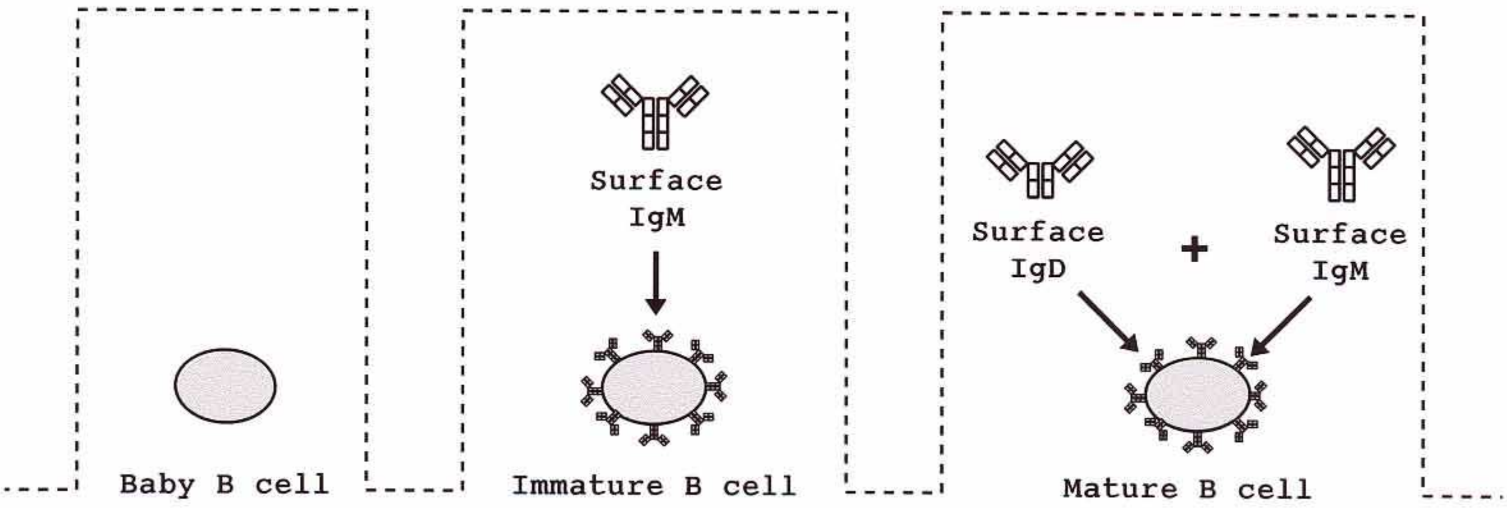


Although the microbes are quickly apprehended, why is it unlikely that these antibodies would have 'grabbed' anything else?

THE STORY STARTS BACK IN THE BONE MARROW

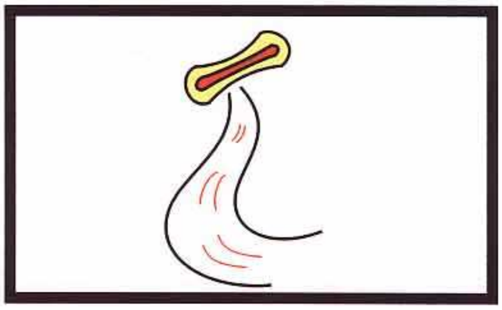


B cells grow and develop inside the bone marrow. Then on reaching maturity, they must leave to find a new home (ie a lymph node).

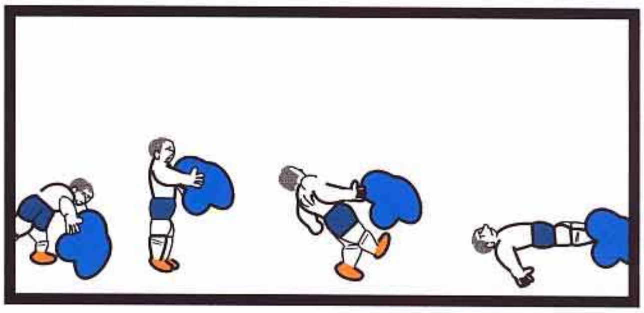


As the B cell matures inside the bone marrow, it expresses a range of surface antibodies.

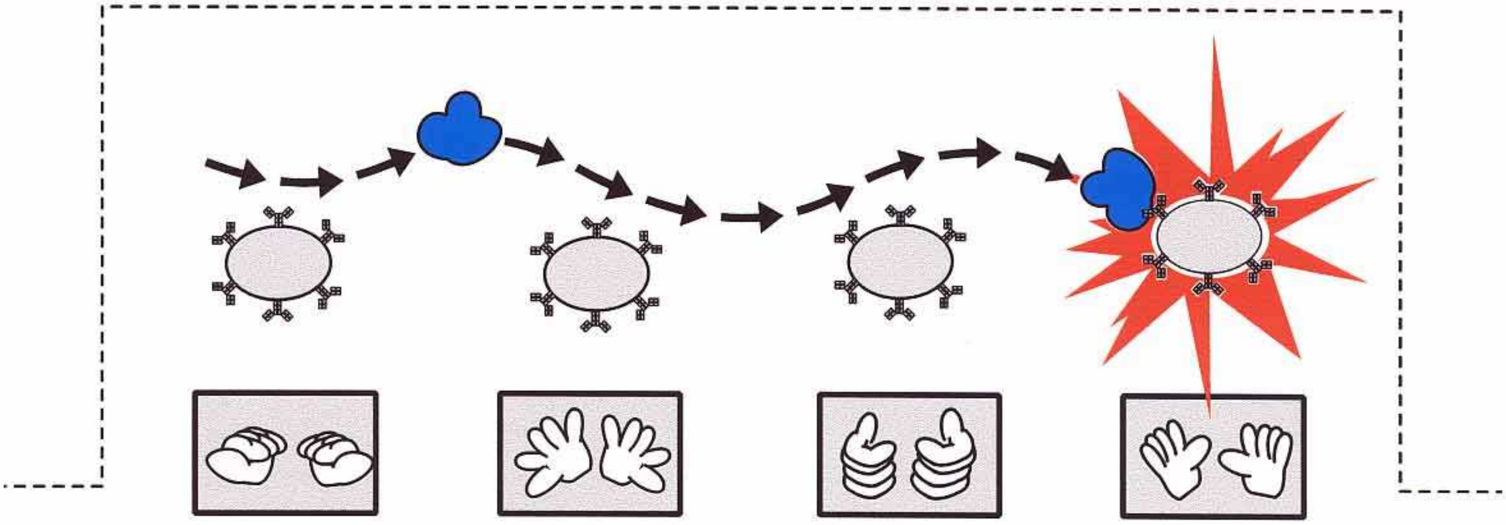
IT'S A QUESTION OF LIFE OR DEATH FOR THE YOUNG B CELL



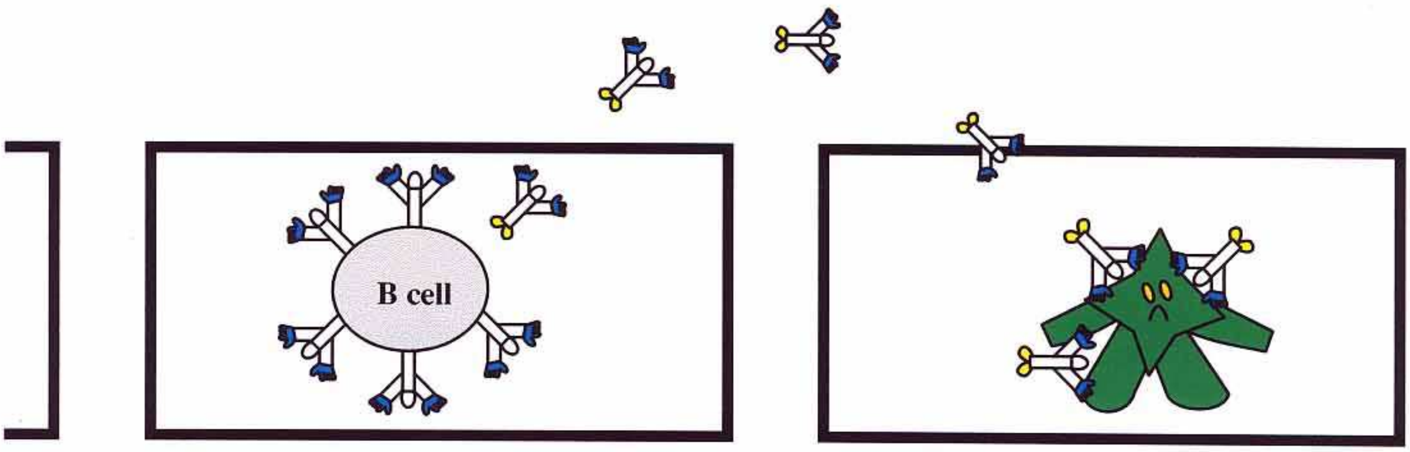
As bone marrow has a good blood supply, many fragments from around the body pass through it.



If an immature B cell's 'hands', happen to fit anything passing through the bone marrow, the B cell auto-destructs.



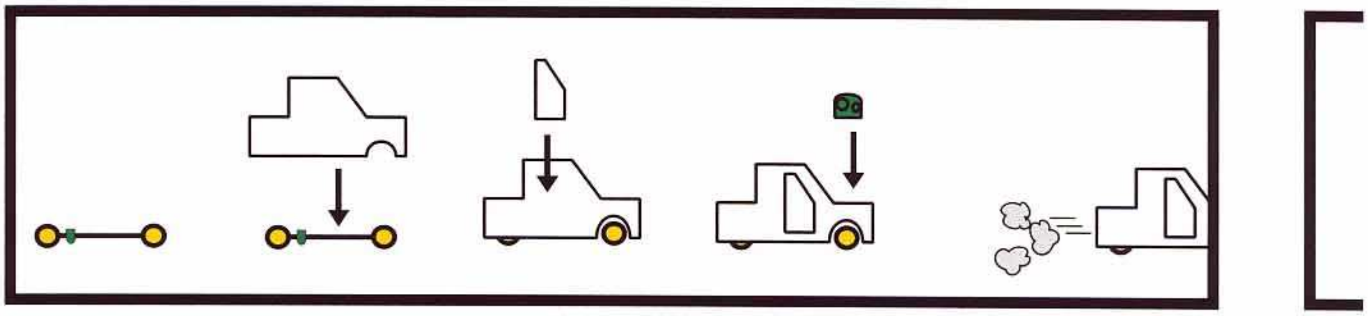
It appears that whilst immature B cells only express surface IgM antibodies, they are at risk of auto - destruction, should their unique fixed 'hand' shape fit anything.



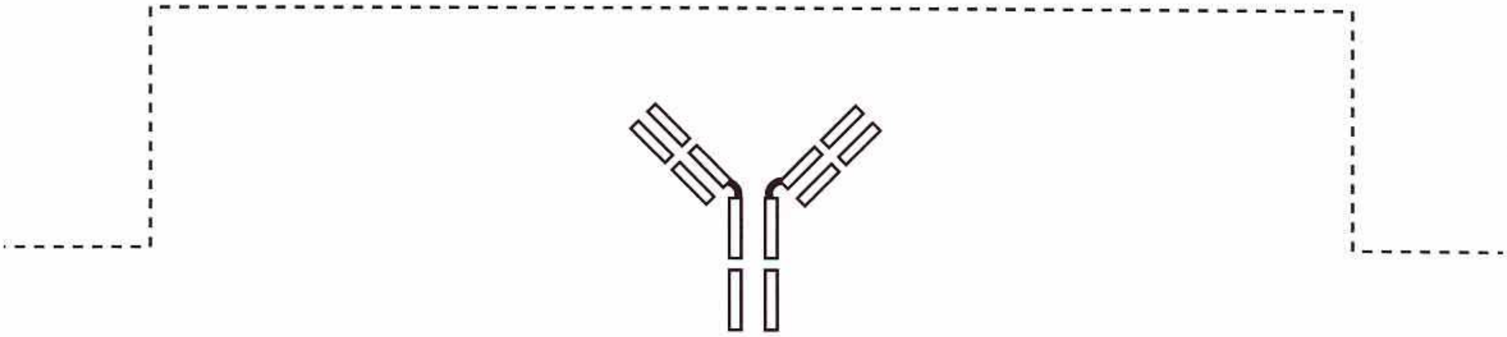
The 'hand' shape of a B cell's surface antibodies, are identical to the antibodies it releases.

It is uncommon for our own antibodies to attack us, because any B cell capable of releasing harmful auto-reactive antibodies, should have died before it could leave the bone marrow.

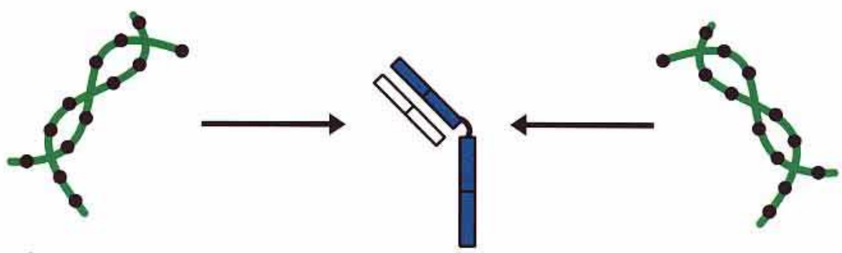
A CAR ASSEMBLY LINE



Parts are bolted together to produce the finished article.

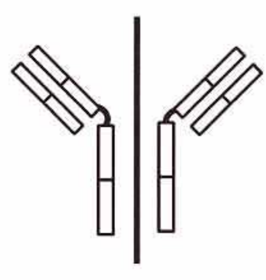


Likewise, antibodies are a number of different parts, 'bolted' together.



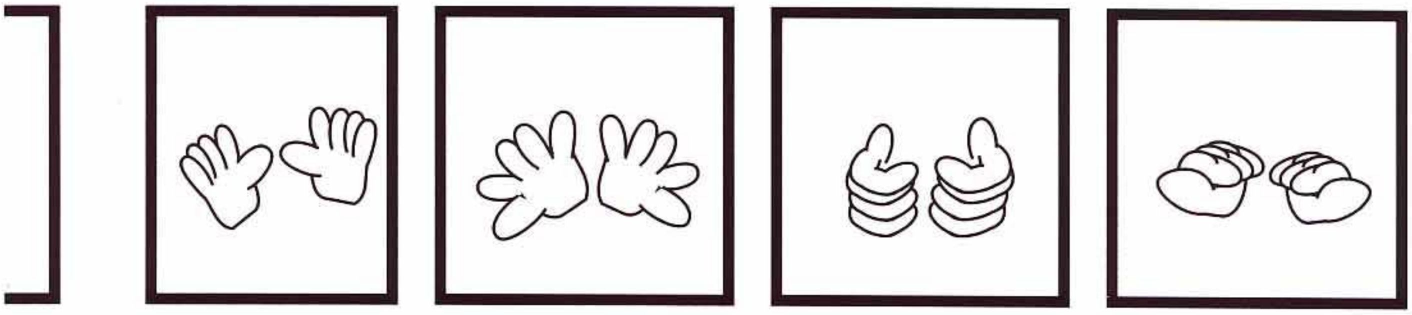
Part of chromosome No.2, codes for the light chain.

Part of chromosome No.14, codes for the heavy chain.

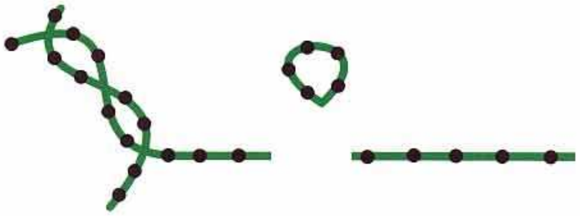


Then 2 identical halves are 'bolted' together.

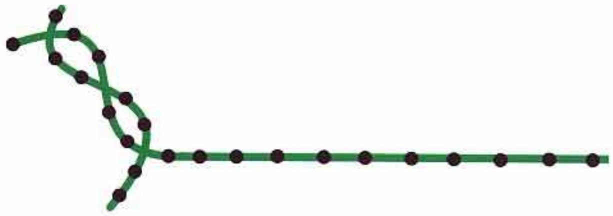
HERE ARE 4 FIXED ANTIBODY 'HAND' SHAPES



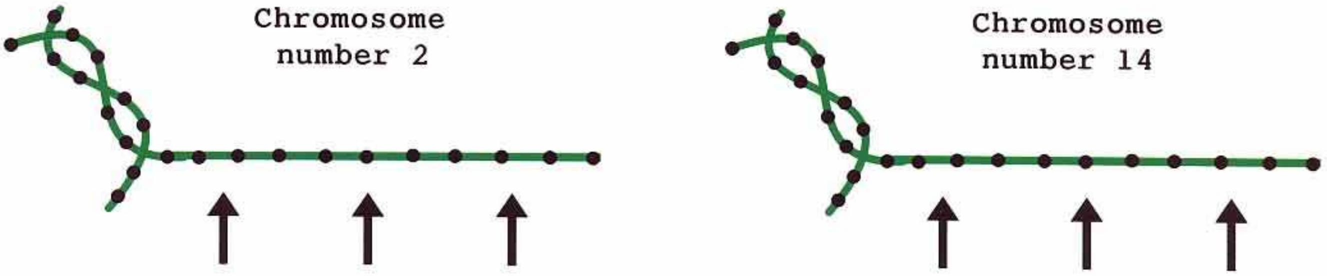
HOW B CELLS ACQUIRE THEIR UNIQUE 'HAND' SHAPE



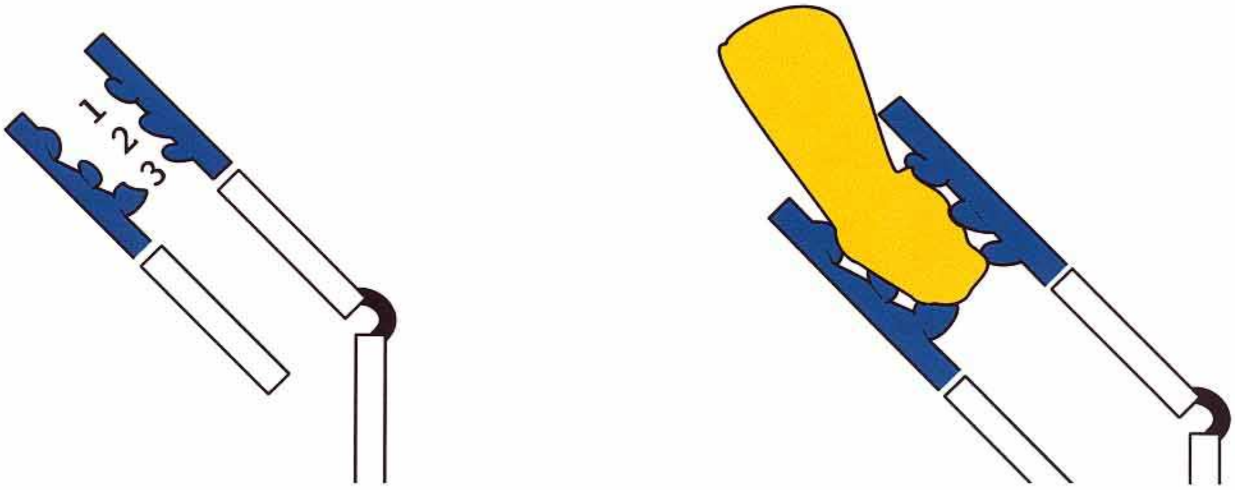
As an immature B cell develops, some of the genes capable of coding for the 'hand' shape, are randomly removed by recombinase enzymes.



The DNA is then rejoined, so that the genes that are left, now code for that B cell's unique fixed 'hand' shape.



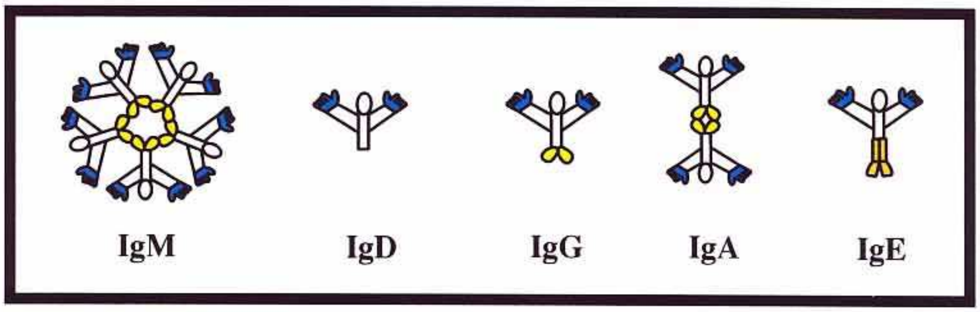
Genes are randomly removed from 3 specific areas along both chromosomes.



This results in 3 unique shapes being produced, along both light and heavy chains.

For the 'hands' to now fit an object, these shapes must conform closely to the object.

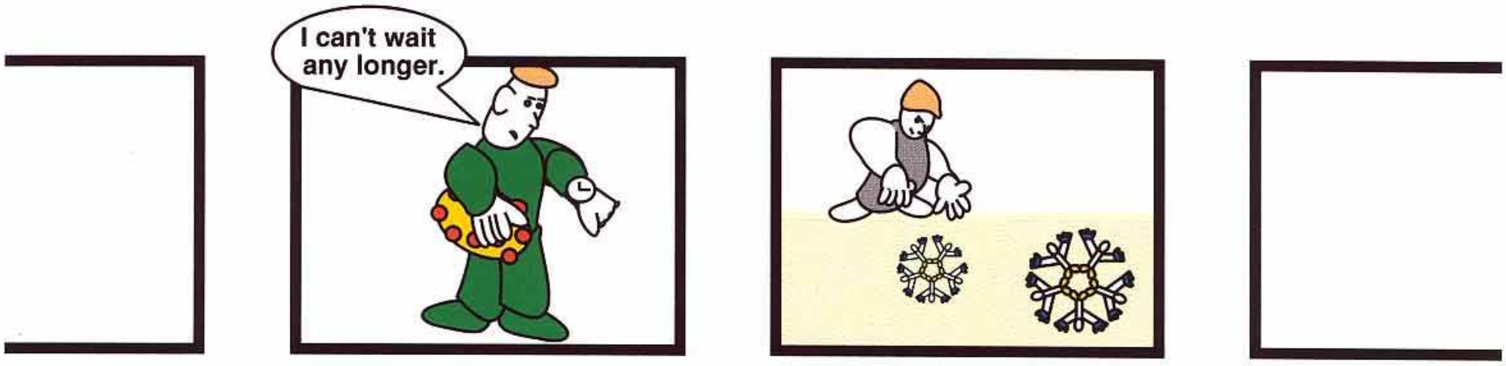
WHO CARES ABOUT CLASS?



There are 5 classes of antibody.

Soluble substances which allow cells to communicate with each other, are sometimes called "cytokines".

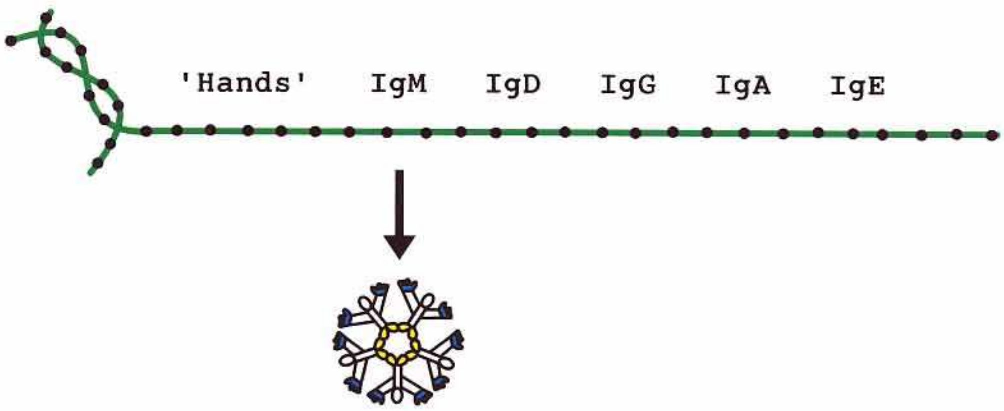
WHEN THE B CELL HAS TO DO THINGS ON HIS OWN



Although this B cell's 'hand' shape fits this object, no T helper cell is to be found.

So after transforming into a plasma cell, he starts to release IgM antibodies.

CHROMOSOME NUMBER 14 INSIDE THIS PLASMA CELL

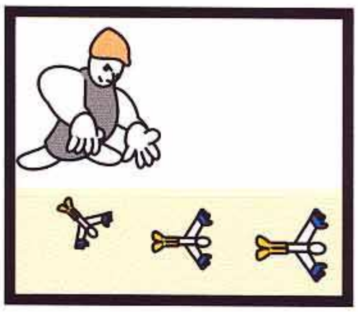


The genes next to those coding for the 'hand' shape, are switched on.

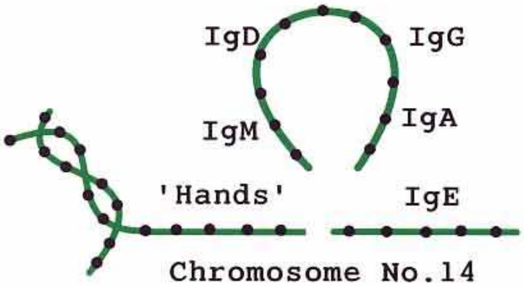
IF A USEFUL T HELPER DOES ARRIVE

This time a T helper arrives, whose 'hand' shape also fits the same object.

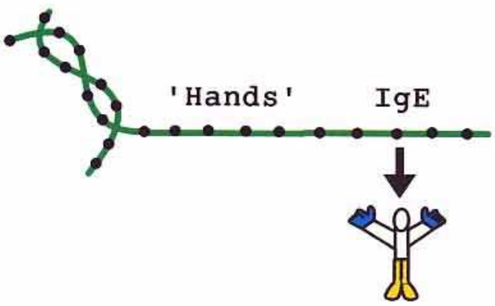
The T helper now releases factors, to make the B cell produce IgE antibodies.



The B cell rapidly transforms into a plasma cell and starts to release IgE.

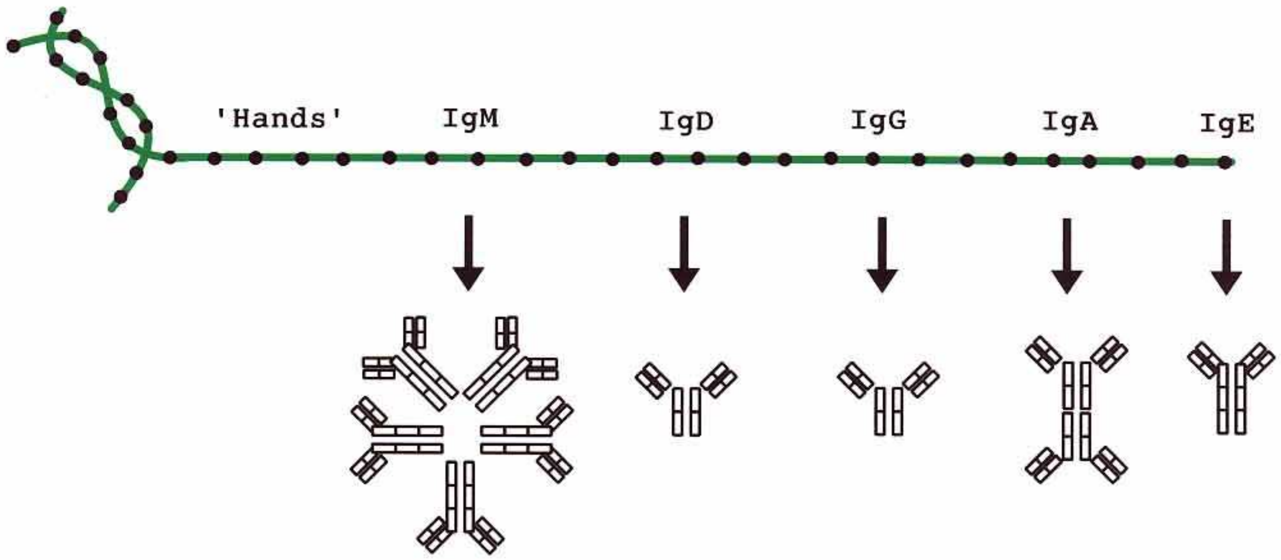


The cytokines from the T helper, trigger enzymes inside the B cell, to remove specific genes along chromosome number 14.



The genes next to those coding for the 'hand' shape, are now switched on.

CHROMOSOME NUMBER 14



A resting B cell is capable of producing any class of antibody. But for a particular class of gene to be activated, a T helper must release specific cytokines such as:- gamma interferon (G.INT) interleukins (IL) and transforming growth factor (TGF).

If the T helper releases IL-2, IL-4, IL-6 and G.INT..IgG are produced.

If the T helper releases IL-2, IL-5 and TGF..........IgA are produced.

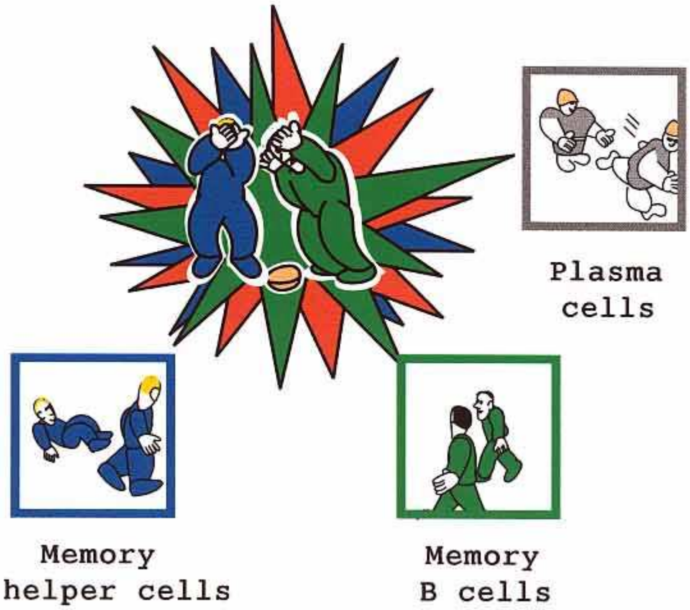
If the T helper releases IL-4.......................IgE are produced.

*IgD antibodies are normally only found attached to the surface of B cells and are not actively secreted into the blood.

THE CLONAL SELECTION THEORY

PRIMARY RESPONSE | SECONDARY RESPONSE

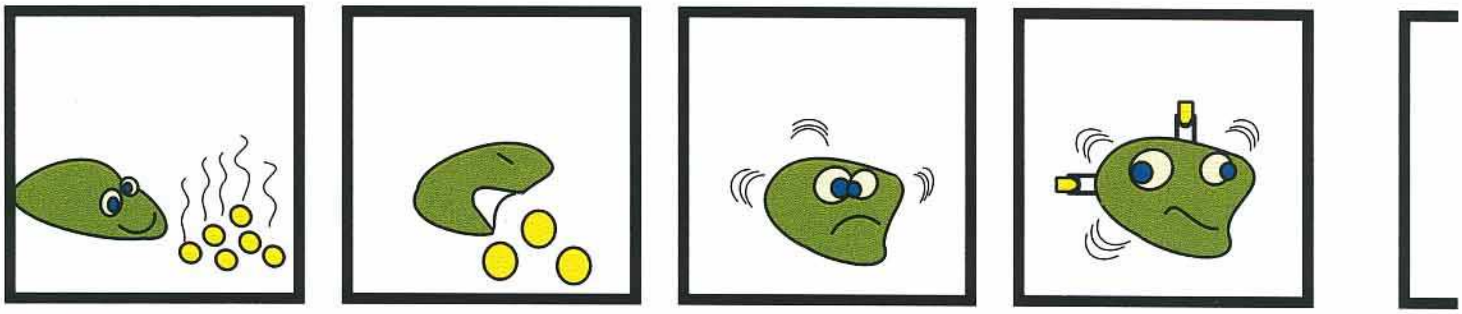
When a microbe appears for a second time, why is there a much larger antibody response?



When a microbe appears for the first time, memory B cells (clones of the original B cell), are produced. These will have identically shaped 'hands', should the same microbe reappear at a later date!

CHAPTER THREE

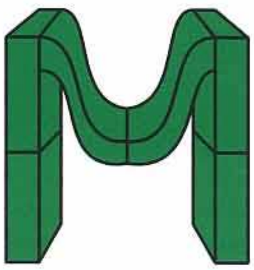
THE 'ATTACK' PROTEIN



When macrophages 'eat' (phagocytose) anything, some of the material appears at the surface, attached to 'attack' proteins. Now their friends can see what they have 'eaten'.

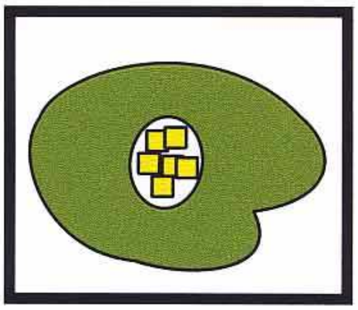
Easy reading

Technical information

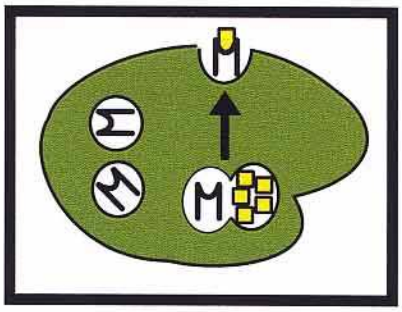


The 'attack' protein's technical (offical) name is the major histocompatibility complex (MHC) class 2 protein.

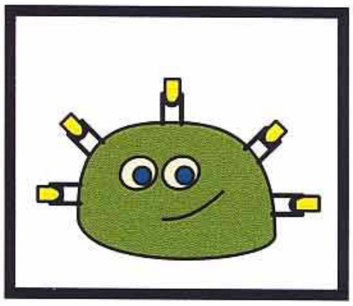
PRESENTING HIS WEARS



Enzymes start breaking down the 'eaten' material.



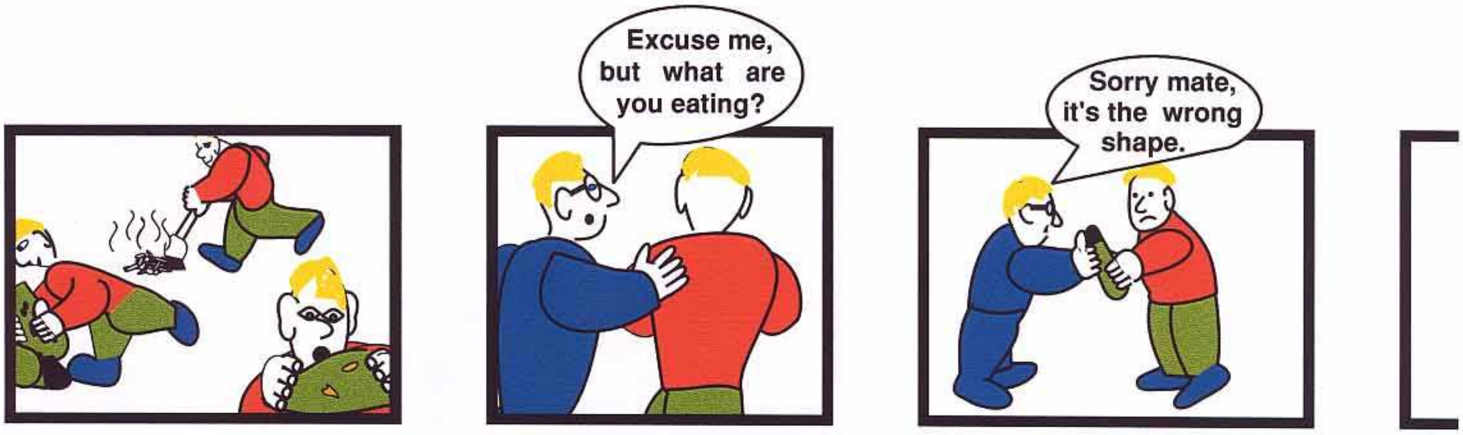
Some of the degraded material is now 'slotted' into the top of the 'attack' proteins.



The complexes are then expressed onto the surface of the cell.

Only small lengths of protein (about 10 amino acids long), can fit into the cleft at the top of the 'attack' protein.

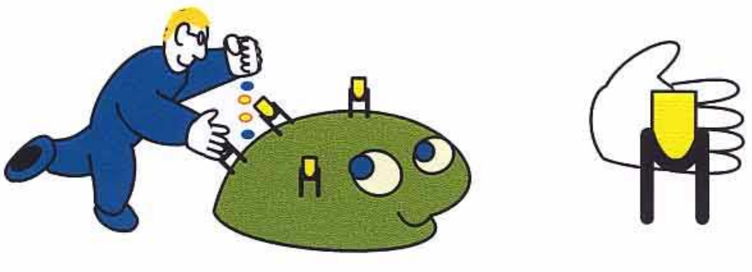
IT'S NICE IF YOU GET A LITTLE EXTRA HELP



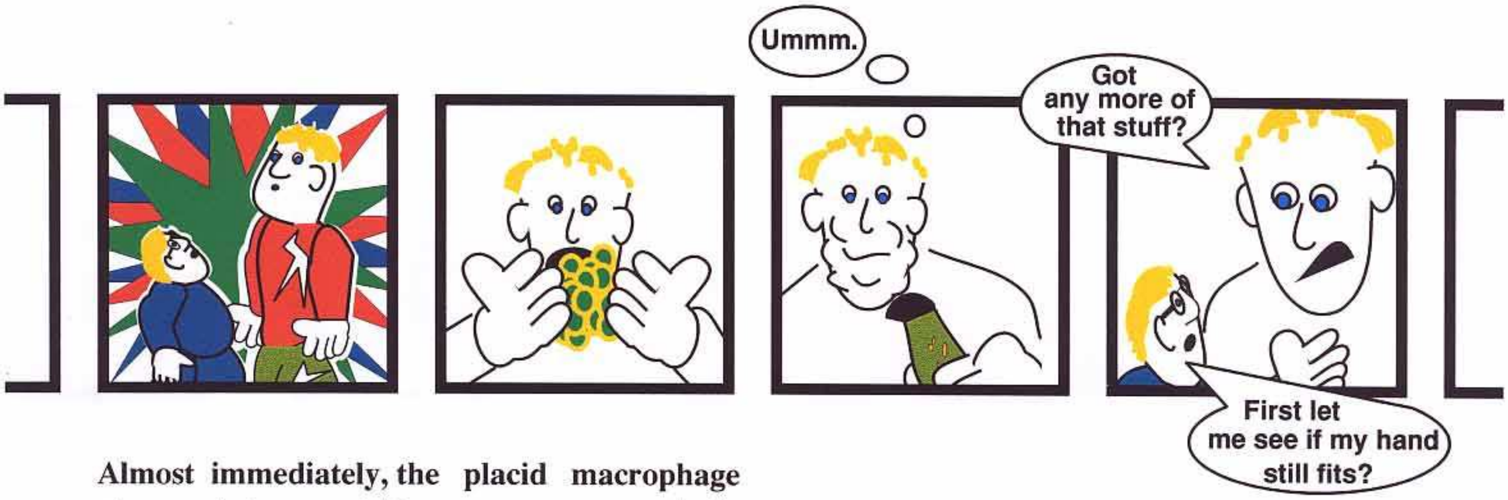
As these macrophages dispose of some waste material, a T helper arrives to see if he can help.

T helper cells can only help if their fixed 'hand' shape fits the presented material.

Wandering over to another macrophage, this T helper cell finds that his luck has now changed.

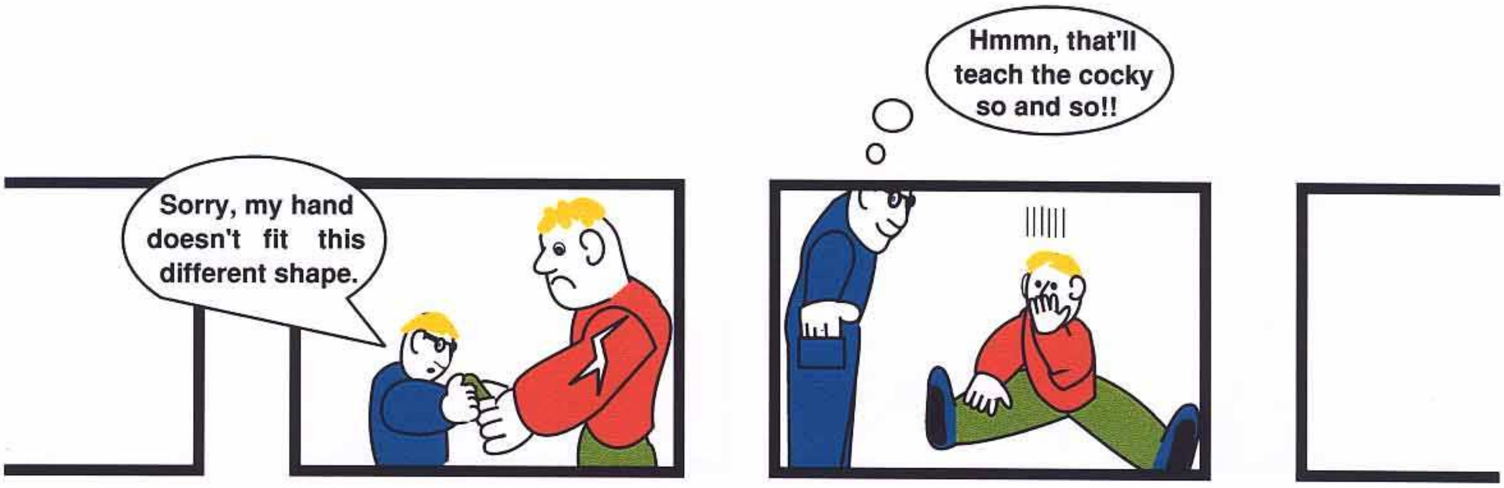


When his 'hand' does fit, the T helper releases cytokines such as:- gamma interferon, interleukin-2, macrophage activation factor and migration inhibitor factor (see page 297).

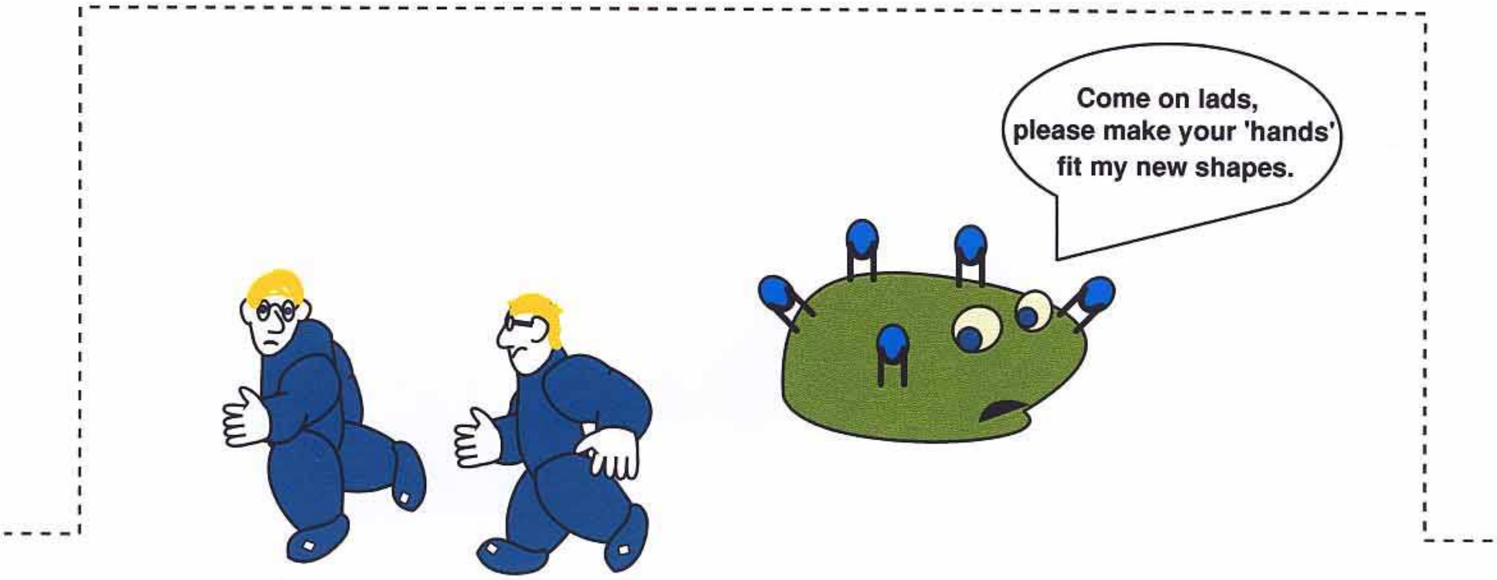


Almost immediately, the placid macrophage changes into a great big, angry, ravenous, hulk.

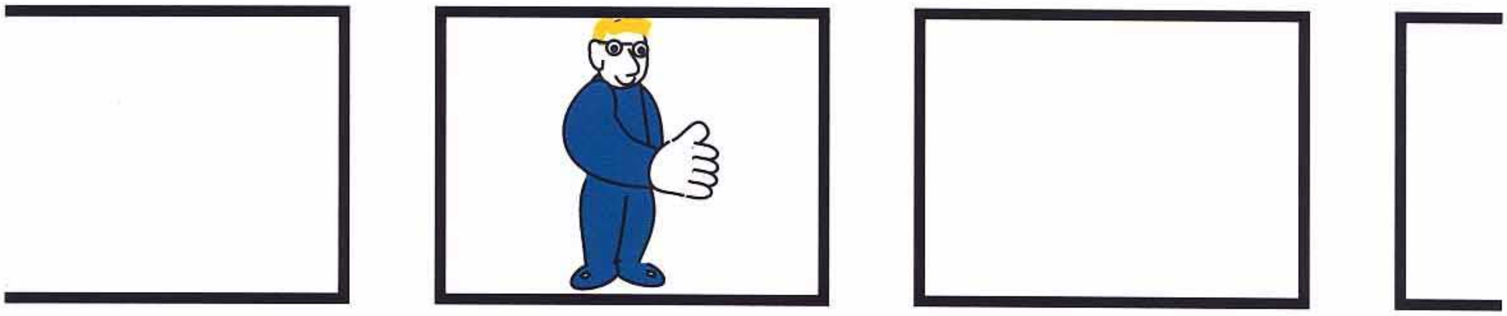
Cytokines from the T helper not only make any macrophages close by very 'angry' and much more efficient at killing microbes, but they also enable the T helper cell to clone itself.



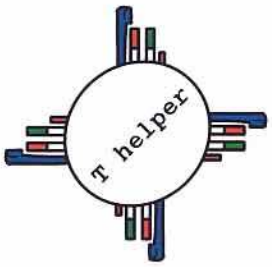
Unfortunately for the macrophage, the effects are only short lived. So once the material has been removed, he will not receive any further stimulation and quickly returns to normal.



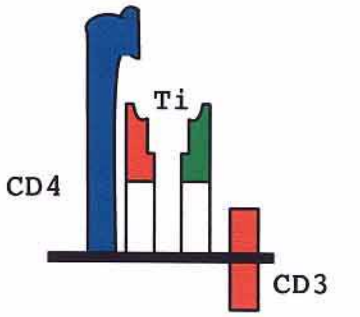
As these T helper clones have identically shaped 'hands', neither can help the macrophage, as it is now expressing a different shaped protein, attached to its 'attack' proteins.



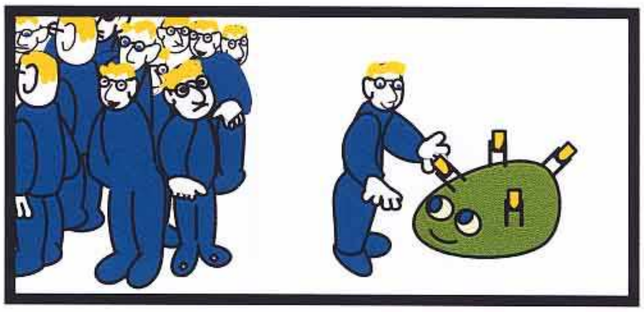
Let's have a closer look at
this T helper cell's 'hand'.



Every T helper cell
has surface receptors
which act like 'hands'.



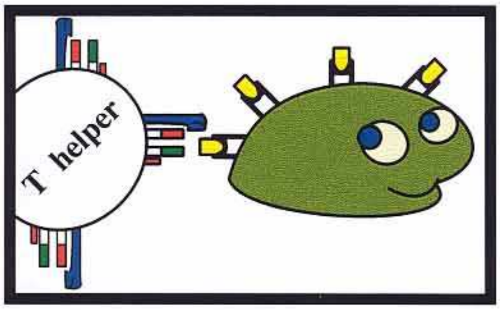
Each 'hand' is made
up of a Ti, CD3 and
CD4 molecule.



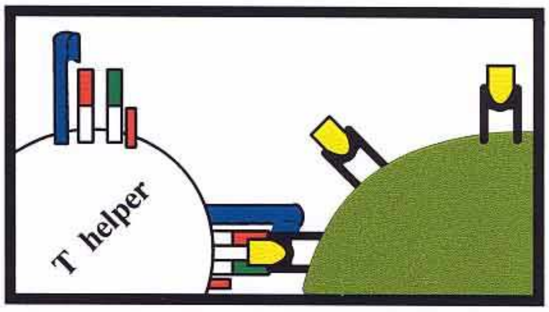
If all these T helper cells have 'hands', why has only one of them been able to 'grab' hold of what this macrophage is presenting?

2 T HELPER CELL 'HAND' SHAPES

Although all T helpers have 'hands' (ie CD3, CD4 and Ti molecules) each has a unique shape at the end of their Ti molecule. It is this which greatly restricts what will fit into its 'hand'.

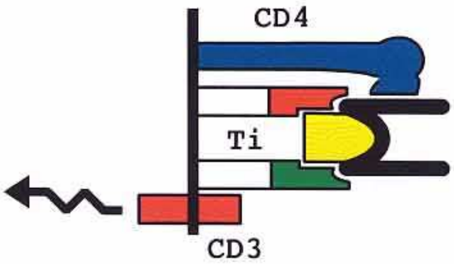


Will this T helper cell's 'hand', fit what the macrophage is presenting?



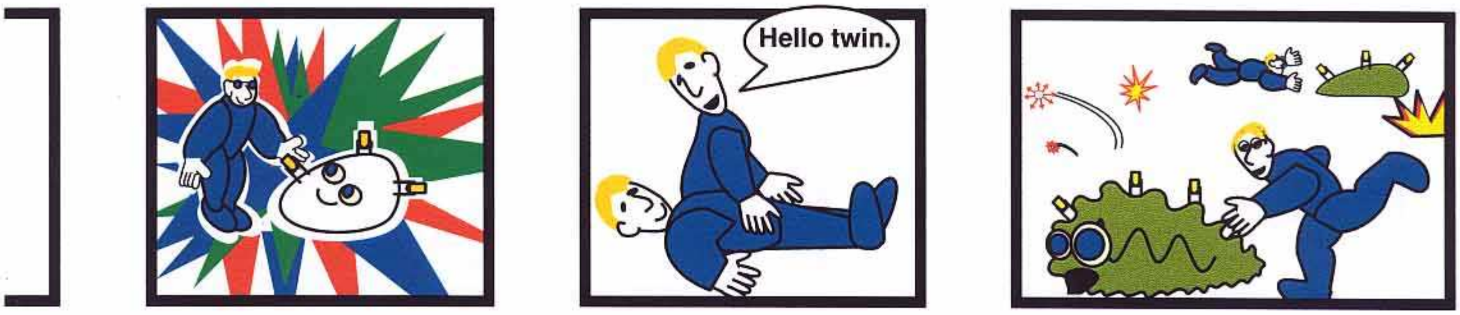
Yes, it's 'hand' fits!!

FOR THAT PERFECT FIT

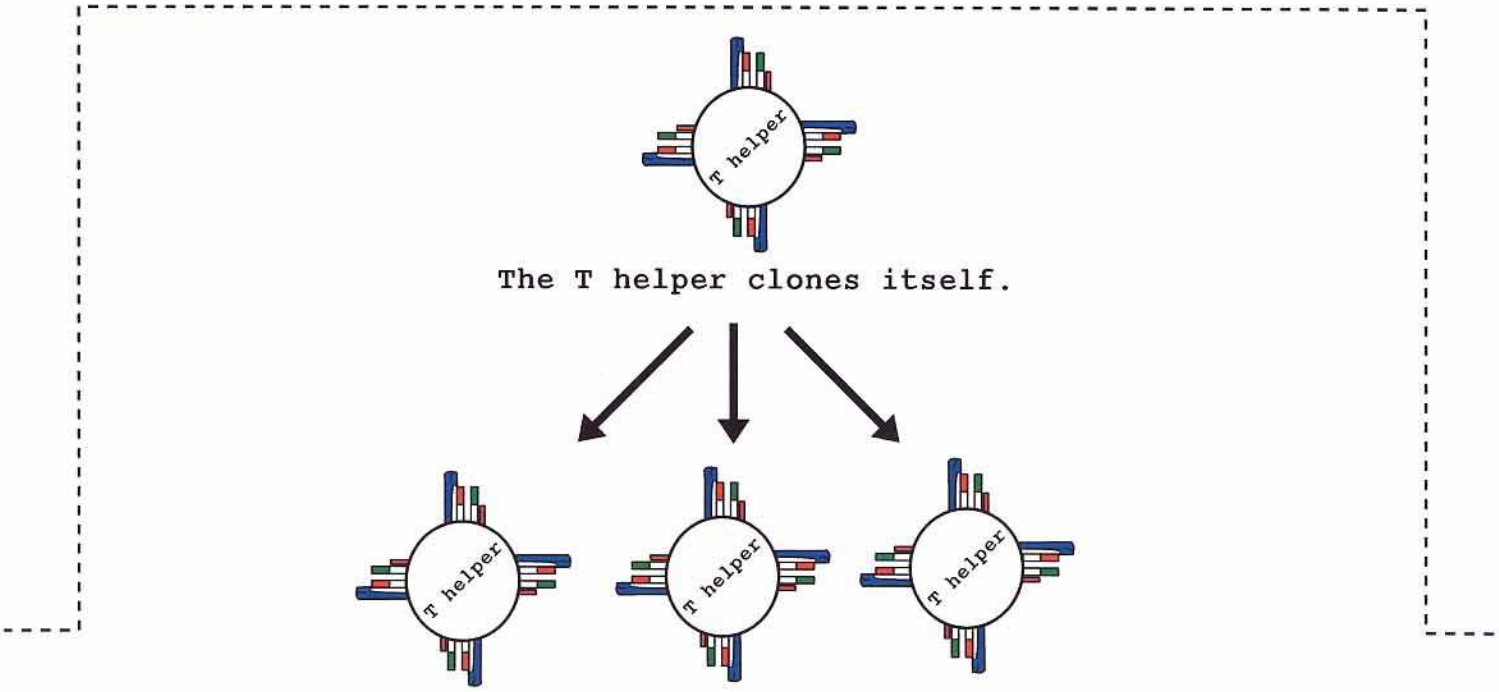


1. CD4 attaches to the side of the 'attack' protein.
2. Ti fits over the top of the 'attack' protein + foreign protein.
3. CD3 can now signal to the nucleus that the 'hand' fits.

ANOTHER EXAMPLE OF THE CLONAL SELECTION THEORY

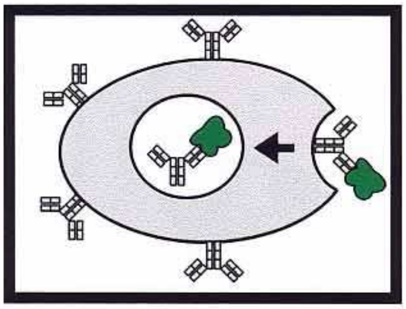


When a T helper's 'hand' fits the presented material, it releases cytokines. These cytokines not only activate any macrophages that are close by, but they also enable the T helper to clone itself.

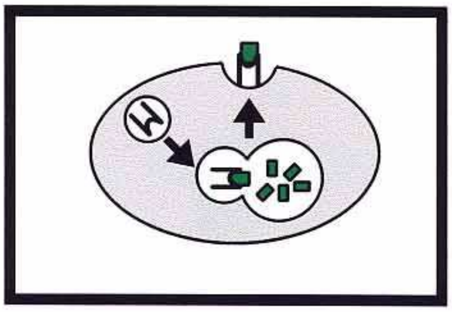


These clones have the same shaped 'hands' as the original T helper. So there are now many more T helper cells ready to respond, should the same foreign material attached to 'attack' proteins reappear.

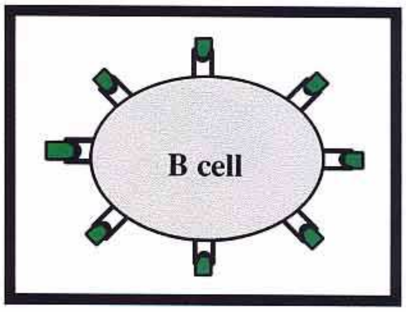
B CELLS AND THE 'ATTACK' PROTEIN



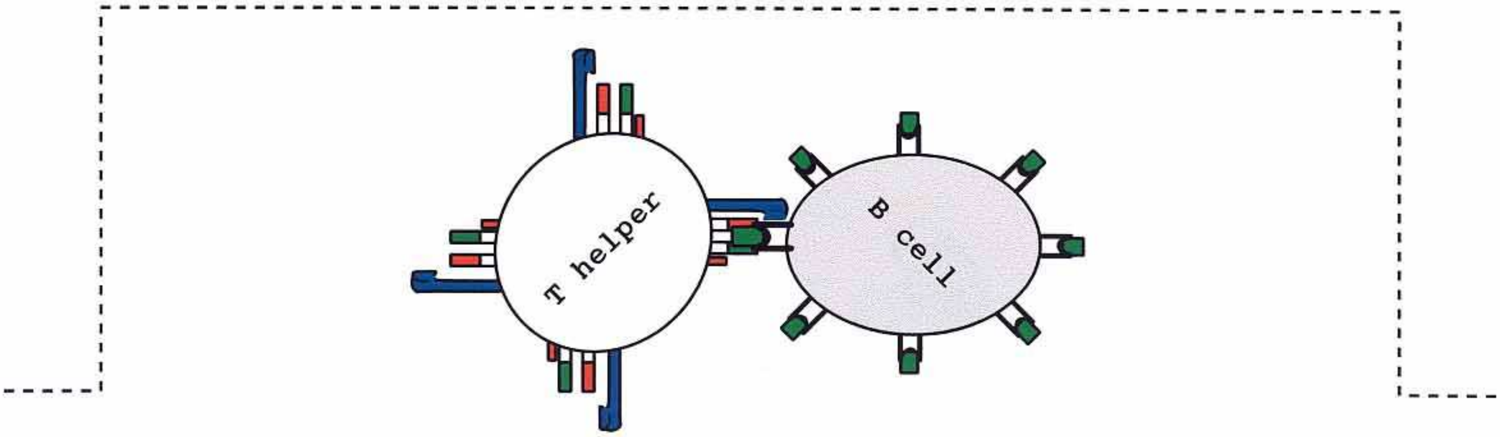
A passing piece of matter attaches onto one of this B cell's surface antibodies.



After being endocytosed and broken down, pieces of it are attached to 'attack' proteins.

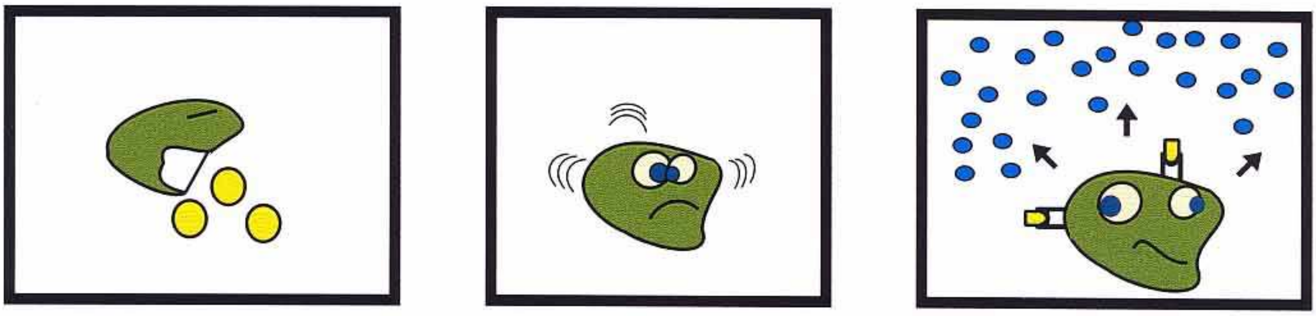


These complexes are now expressed onto the surface of the B cell.

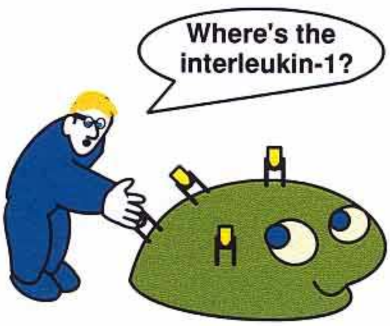


Here we see a T helper with the right shaped Ti receptor. Apart from macrophages and B cells, few other cells in the body routinely express the 'attack' protein.

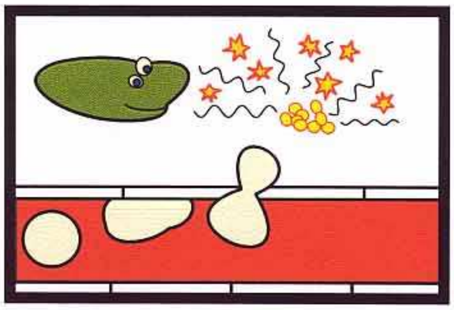
THE SECOND SIGNAL



When material is expressed onto their surface, macrophages should also release interleukin-1.

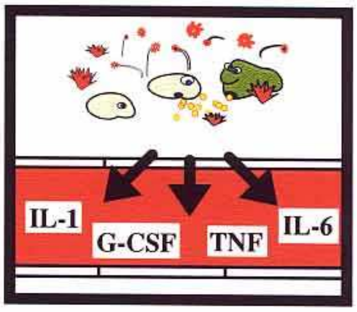


Although this T helper's 'hand' fits, if the macrophage doesn't release interleukin-1, the T helper cell cannot release any cytokines.



On detecting trouble, resident macrophages and circulating neutrophils go to investigate.

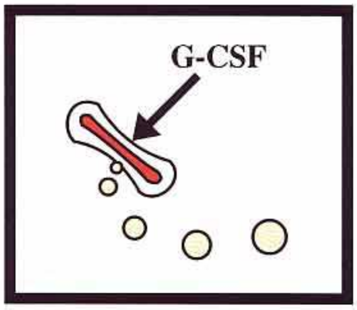
These immune cells will attempt to eliminate the invading microbes.



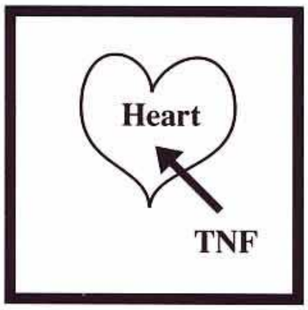
Cytokines released into the blood, will summon up extra help!!

G-CSF : Granulocyte colony-stimulating factor
TNF : Tumour necrosis factor
IL-1 : Interleukin-1
IL-6 : Interleukin-6

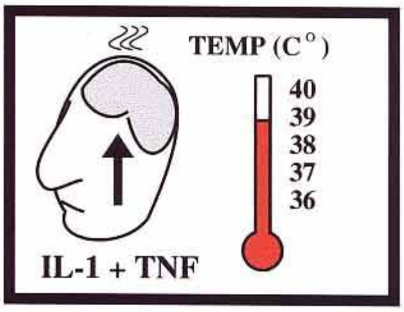
SYSTEMIC RESPONSES TO BACTERIAL INFECTIONS



G-CSF increases the bone marrow's output of neutrophils.



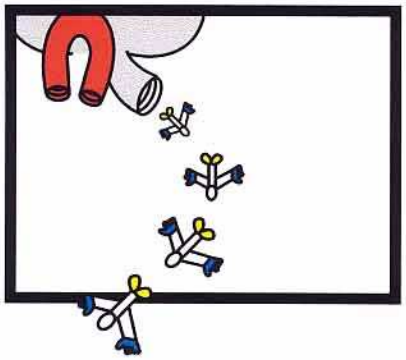
High levels of tumour necrosis factor, will affect heart rate.



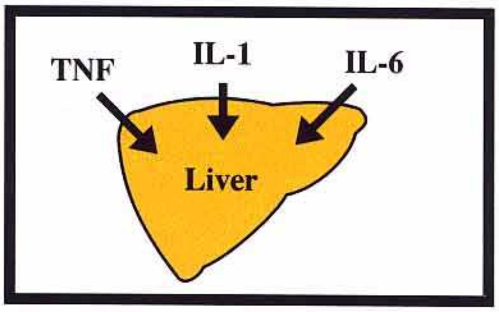
IL-1 and TNF triggers the hypothalamus into making prostaglandins, which will raise the body's temperature.

The larger the infection → The greater the release of cytokines → The greater the systemic response

High levels of TNF can actually be life threatening (see page 103).



Antibodies are released.



Raised levels of IL-1, TNF and IL-6, trigger an acute phase response from the liver.

THE ACUTE PHASE RESPONSE

The liver releases increased amounts of:-

Alpha 2 macroglobulin

C-reactive protein

Fibrinogen

The increased release of fibrinogen into the blood, causes a raised erythrocyte sedimentation rate.

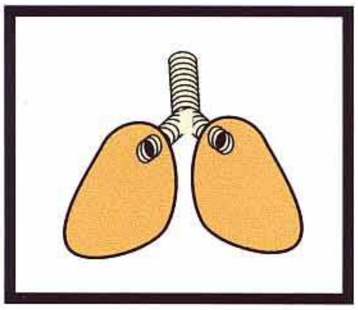
The liver releases decreased amounts of:-

Albumin

Transferrin

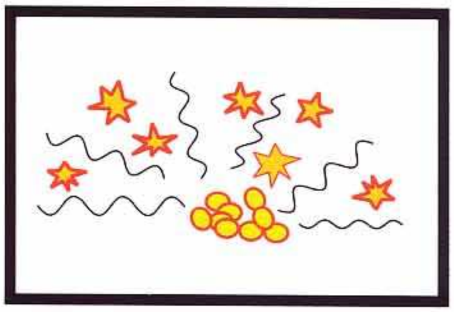
The decreased release of transferrin into the blood, deprives any replicating bacteria, of a ready supply of iron.

WHY IS INFECTED SPUTUM GREEN?

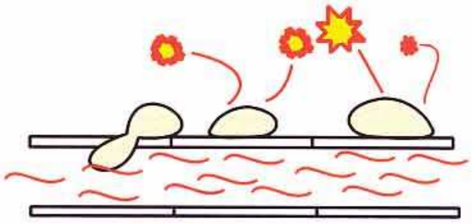


Normally our lungs only produce a small amount of watery mucus.

Suddenly you catch a cold and start to cough up thick green sputum.

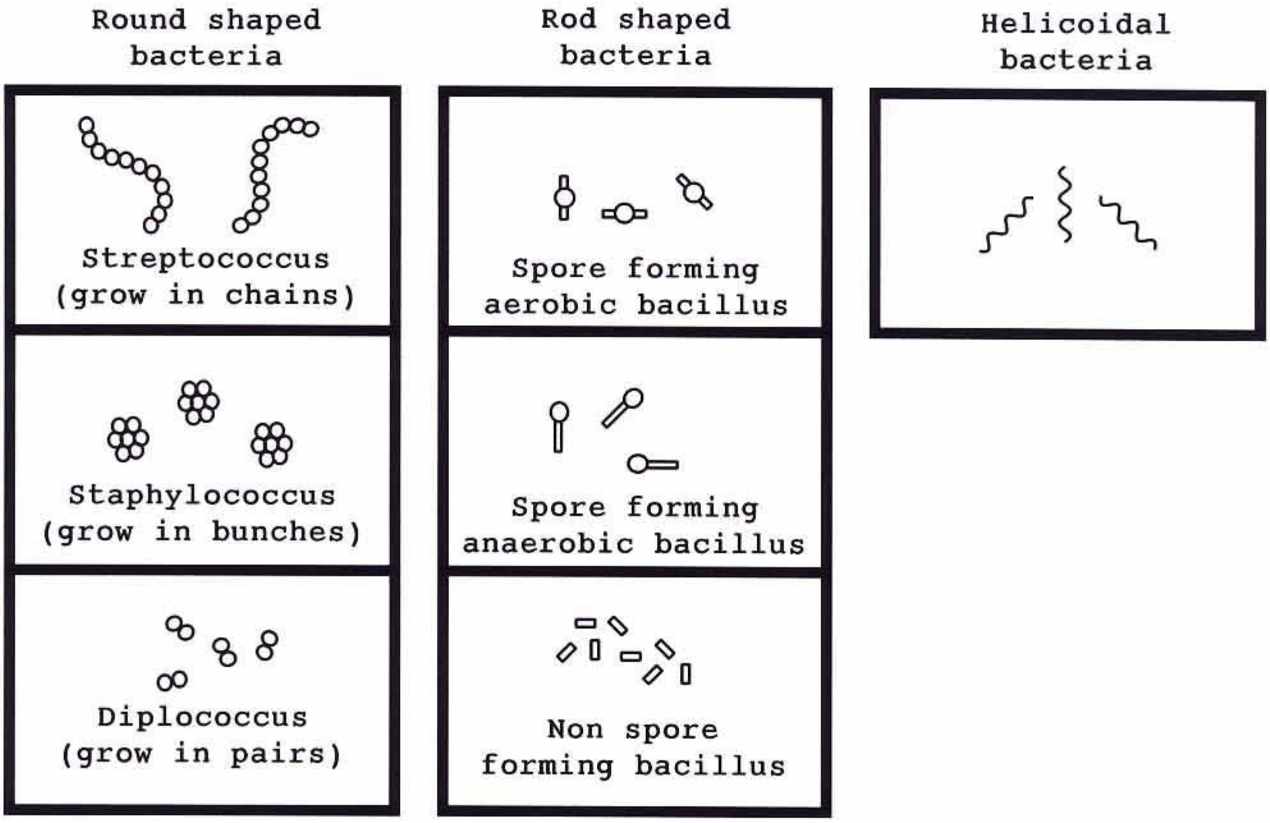


Inflammation released during a bacterial infection, stimulates excessive mucus production.

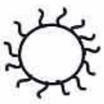


Neutrophils entering the lungs, use emzymes to kill the bacteria. Some of the enzymes contain copper and it is this which turns the mucus in the lungs green.

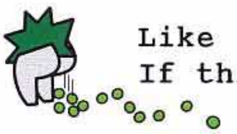
BACTERIAL CLASSIFICATION



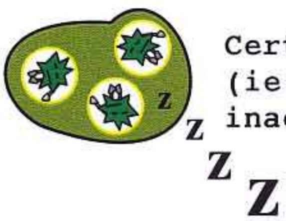
Gram-positive bacteria have a thick cell wall, made up of peptidoglycans which absorbs the gram stain.



Gram-negative bacteria have a thin cell wall, which does not absorb the gram stain. Attached to the cell wall are endotoxins (lipopolysaccharides) which are released when the bacteria dies and can be very toxic.



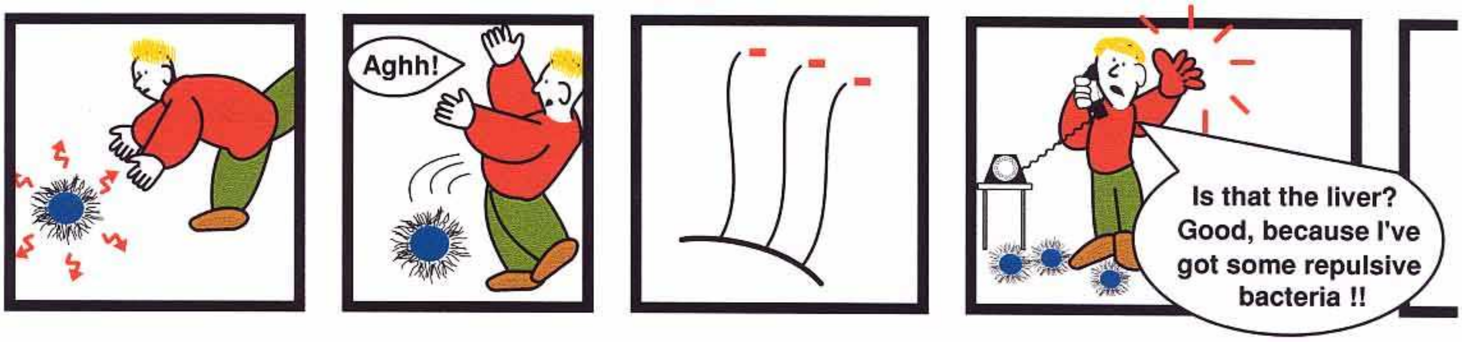
Like all living things, bacteria produce waste. If this then causes disease, it is called "exotoxins".



Certain bacteria produce spores in adverse conditions (ie a lack of heat or moisture). These can then remain inactive for a long time until conditions improve!

GROUP A STREPTOCOCCAL BACTERIA

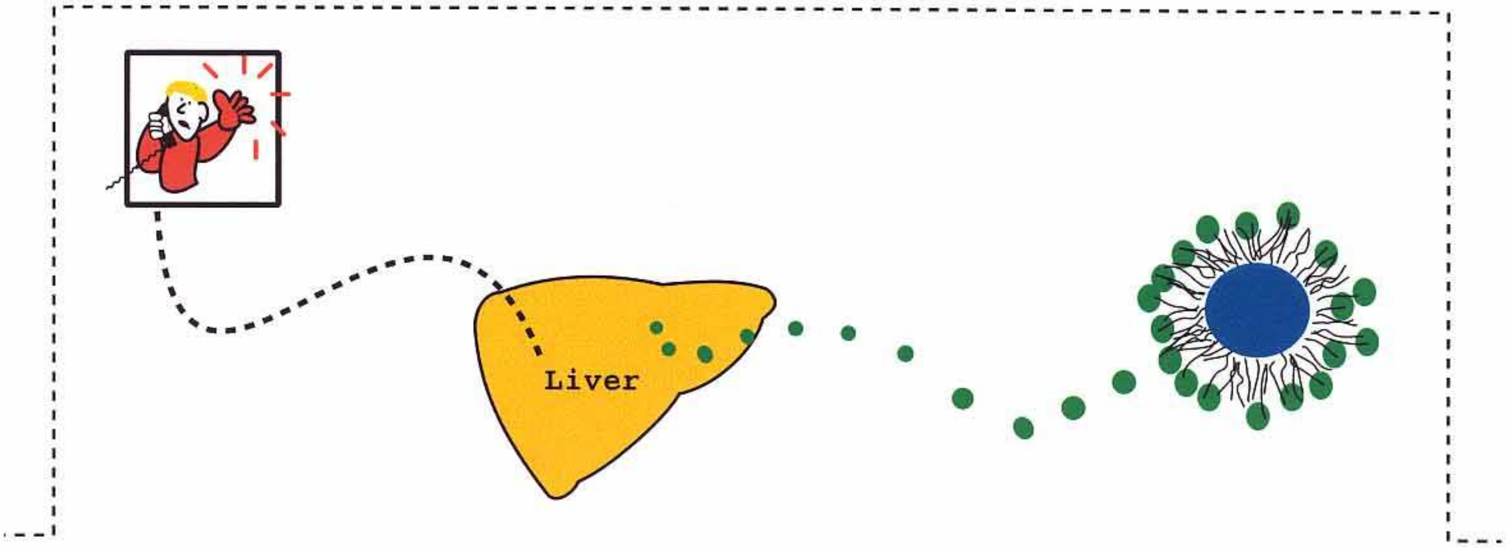
This bacteria is covered in M proteins, giving it an unusual 'hairy' appearance.



Stooping down to pick up a 'hairy' bacteria, this macrophage gets a nasty electric shock!!

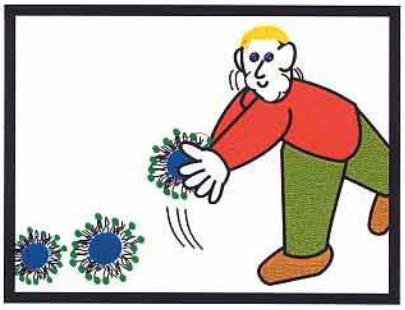
A negative charge is found at the tips of the 'hairs'.

Finding that he is unable to pick it up, the macrophage calls up the liver.

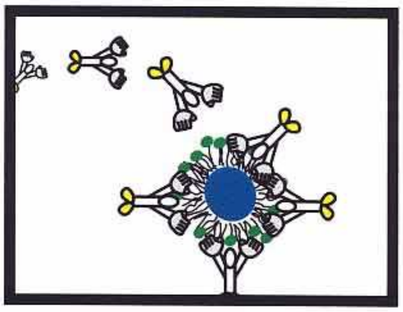


When macrophages encounter this type of bacteria, they release factors which are carried by the blood to the liver.

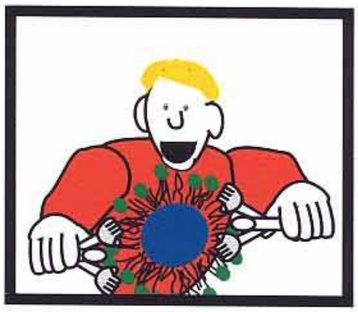
The liver responds by releasing opsonins, which attach onto the ends of the M proteins and neutralise its negative charge.



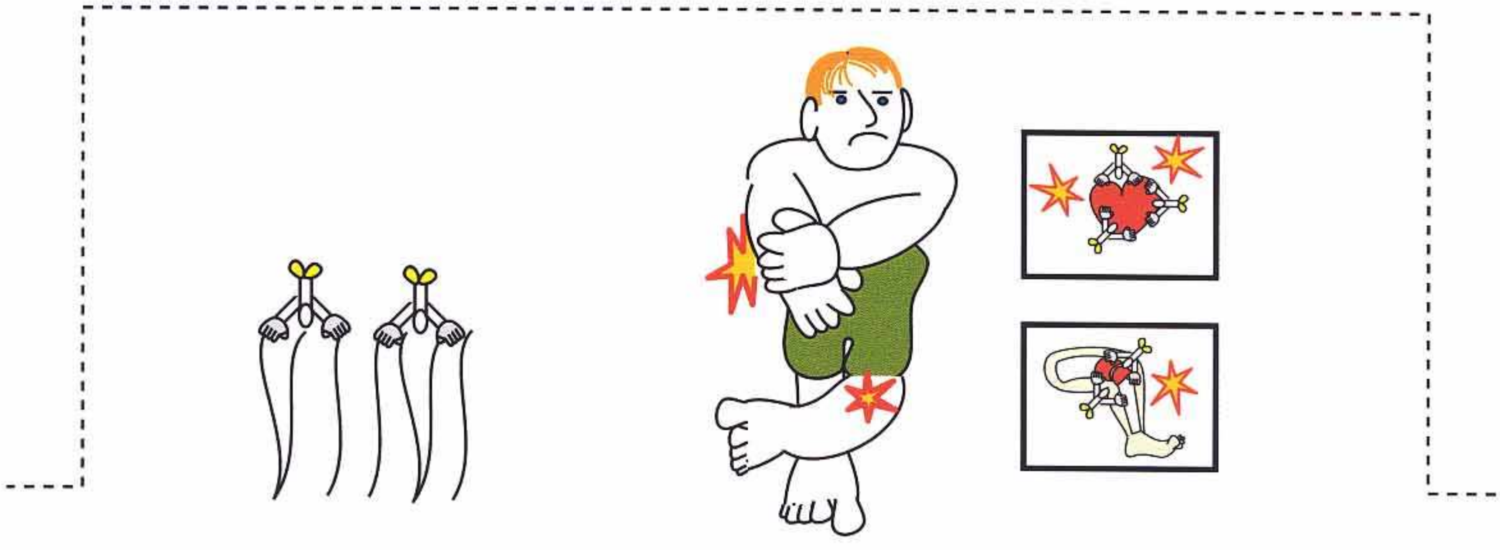
Once coated in opsonins, the 'hairy' bacteria can now be picked up and 'eaten'.



It is not long before IgG start arriving and they too, latch onto the M proteins.



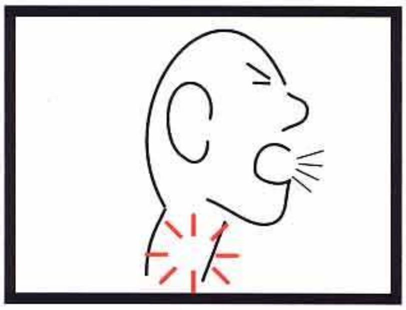
These help to make his job even easier!!!



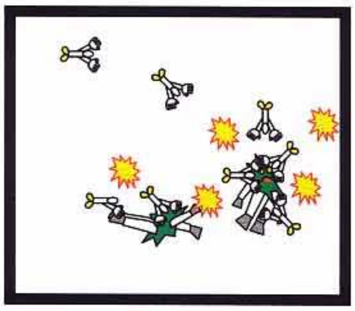
Unfortunately for some children, these antibodies not only 'grab' the M proteins, but they also attach onto the child's joints and heart muscle. This can be life threatening (see page 62).

ACUTE GLOMERULONEPHRITIS

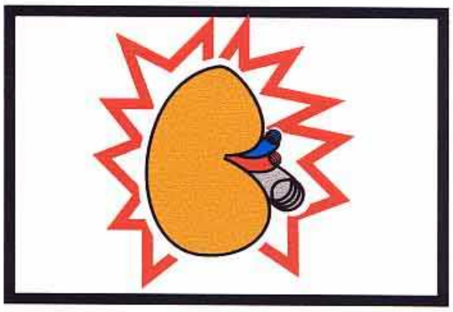
This condition can occur, following a haemolytic streptococcal bacterial infection, somewhere in the body.



Mr Ivor Sorethroat's cough, is due to a haemolitic strepto-coccal bacterial infection.

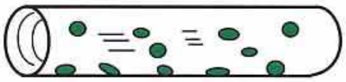


After a couple of weeks, antibodies appear and eliminate the bacteria.



But as his sore throat improves, Ivor starts having excruciating kidney pains.

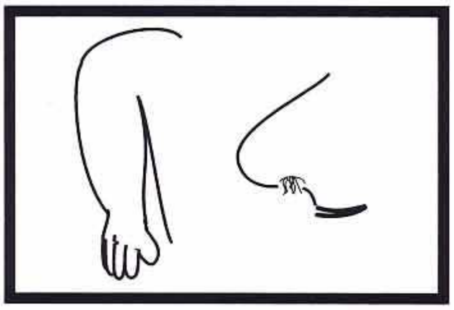
SO WHAT WENT WRONG?



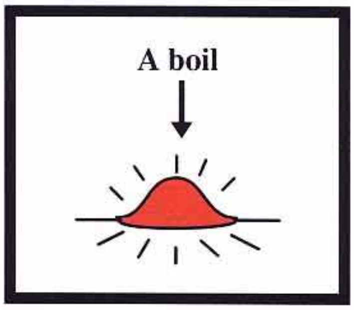
When the sore throat began, pieces of the bacteria became attached to the walls of the glomeruli inside the kidneys.

2 weeks later, antibodies attach onto the bits of microbe in the kidneys, activating complement and neutrophils.

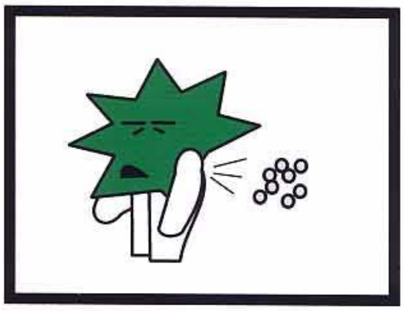
STAPHYLOCOCCAL BACTERIA



Staphylococcal bacteria live in places like our arm pits and nose, where they cause few problems.



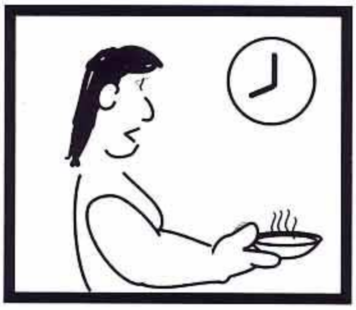
But if they get under the skin, a superfical infection like a boil can develop.



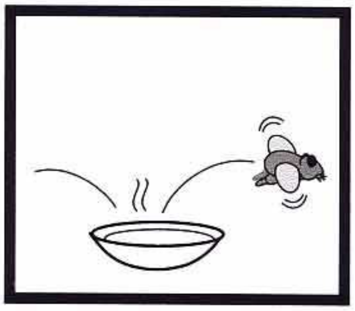
Certain strains of staphlylo-coccal bacteria, release nasty waste products (toxins).

As Mr Jeckyll, they are useful commensals (see page 3). But as Mr Hyde, they can be dangerous pathogens, causing such things as:- osteomyelitis, pneumonia and septicaemia.

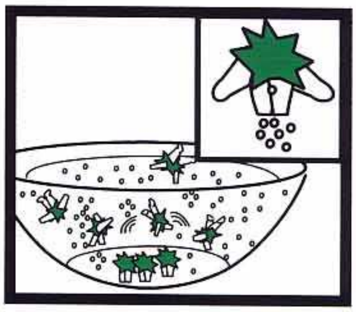
FOOD POISONING



Jackie leaves out a hot bowl of soup to cool down in the open.

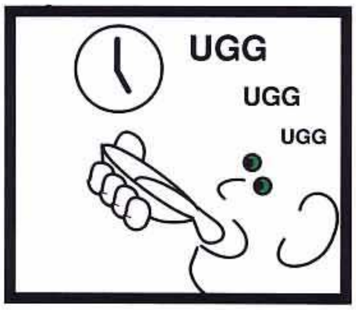


Unfortunately, while she is out of the room, it becomes contaminated.

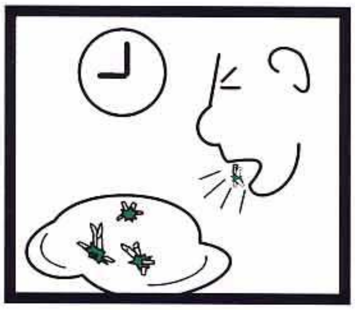


Staphylococcal bacteria start to replicate and release enterotoxins.

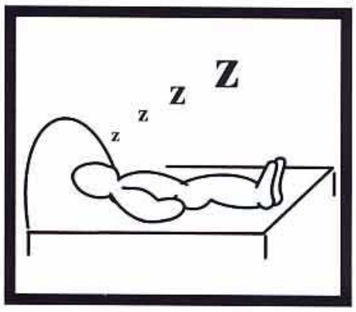
```
Food contaminated with bacterial enterotoxins is
a poison and if eaten, must be expelled  quickly.
```



Sometime later, Simon returns home and gulps down the soup.

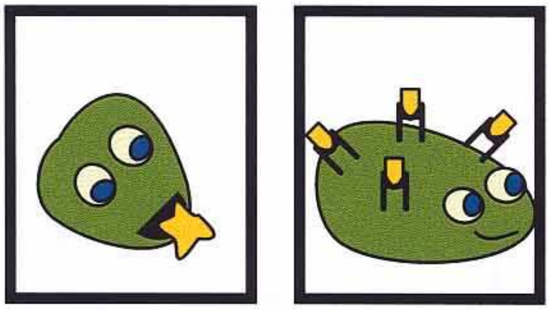


That evening he is sick.

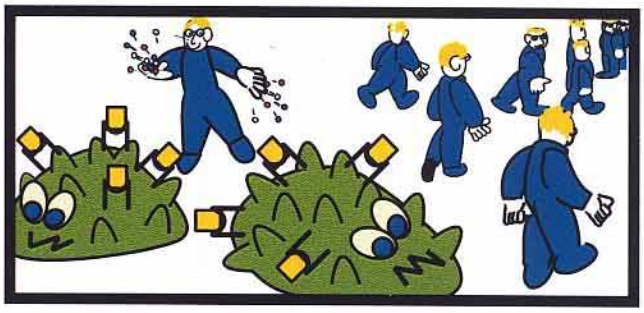


But once the toxins have been expelled, things can then get back to normal.

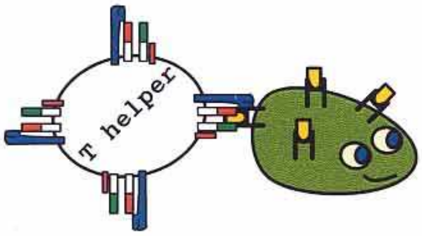
How is the body able to expel food contaminated with enterotoxins so quickly?

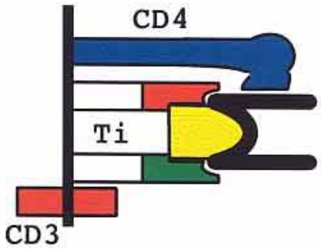


After 'eating' waste material, small pieces are normally expressed, attached to 'attack' proteins.



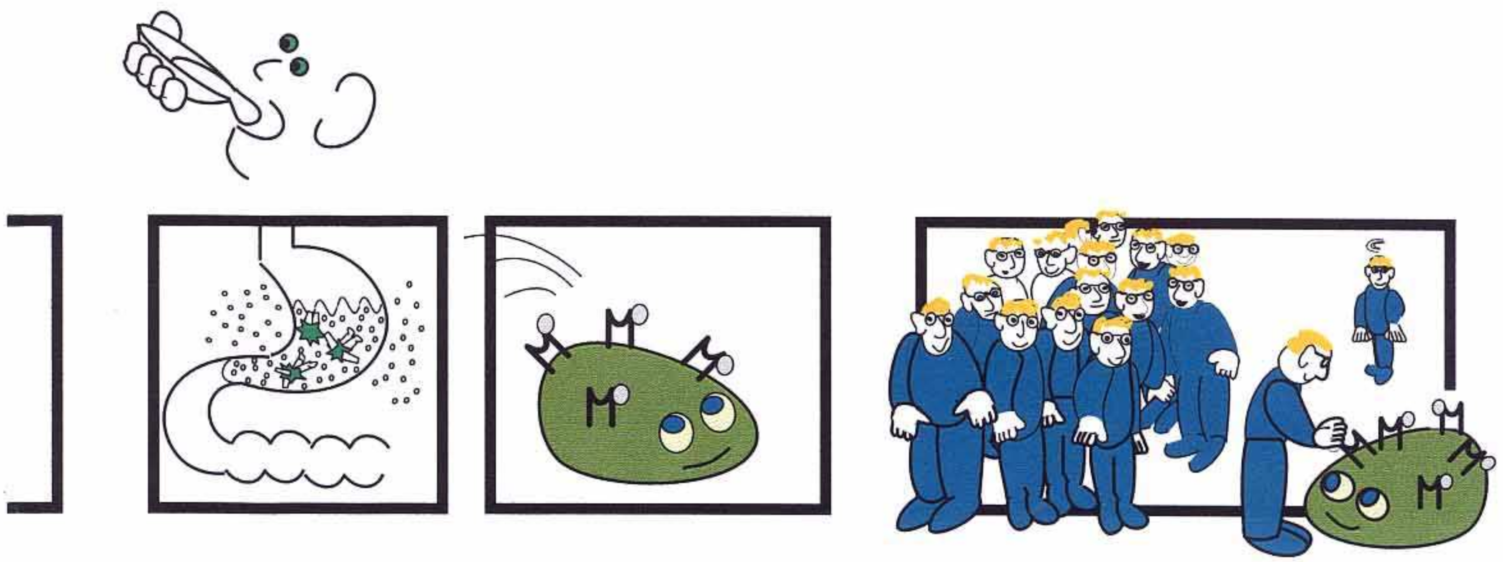
Although many T helper cells then want to help, most of them have the wrong shaped 'hand' and are disappointed!





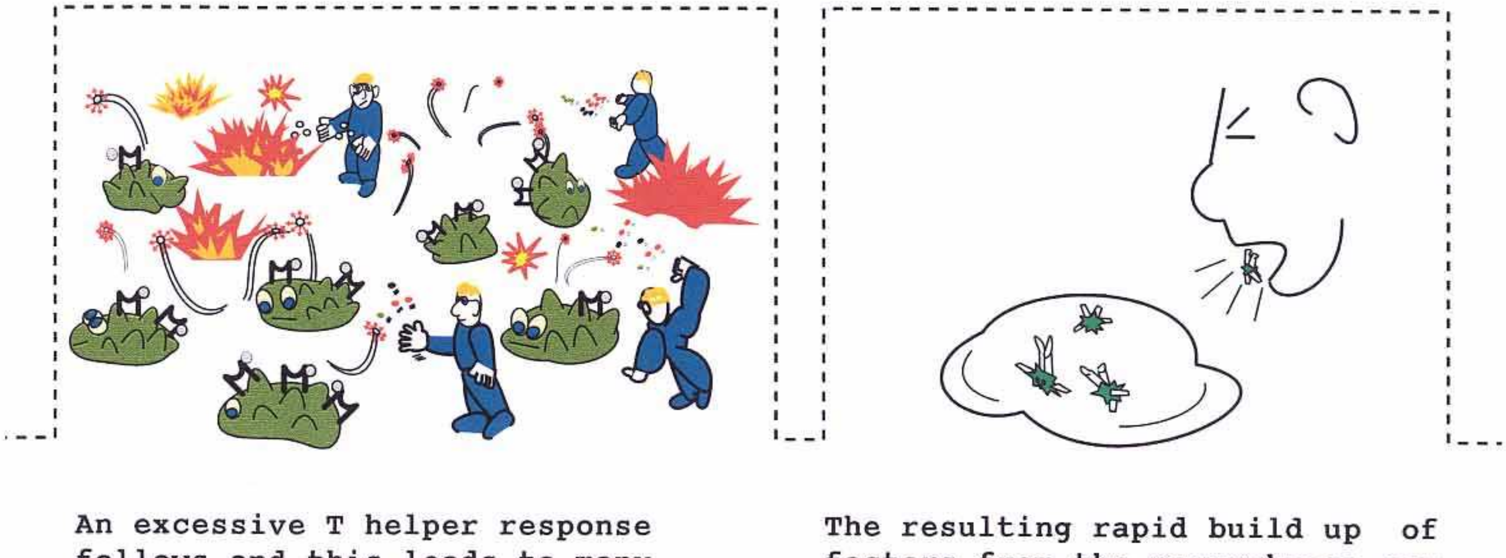
Normally, the T helper's Ti shape (see page 85), is all important.

SO WHY IS CONTAMINATED FOOD EJECTED SO QUICKLY?



Enterotoxins enter the stomach and rapidly diffuse into the tissues. They then attach onto the outside of the 'attack' proteins, without first being 'eaten'.

Many more T helper cells, now find that their 'hand' shape fits the 'attack' protein + enterotoxin.

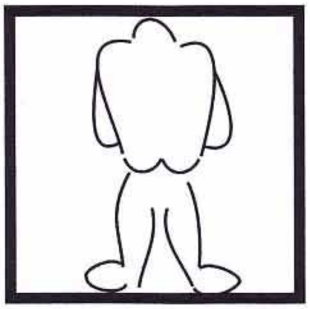


An excessive T helper response follows and this leads to many more macrophages than normal being galvinised into action.

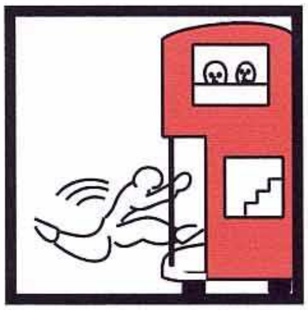
The resulting rapid build up of factors from the macrophages now causes the stomach to violently expel the contaminated food.

TOXIC SHOCK SYNDROME

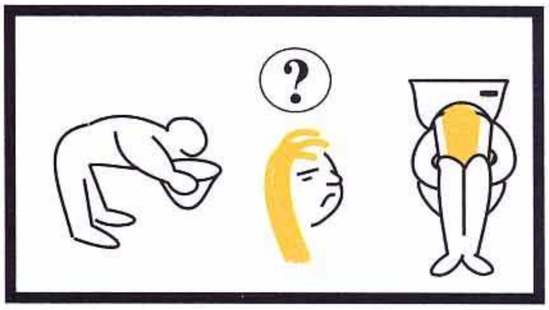
A potentially lethal condition.



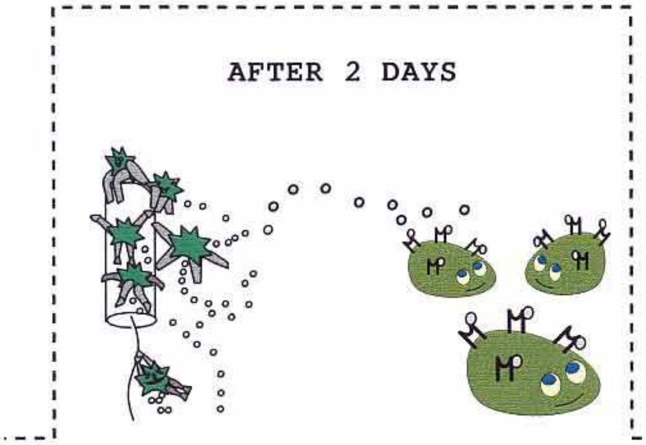
This morning, Beccy realises she is going to need a tampon.



Then it is off to work and she forgets about her tiny package!



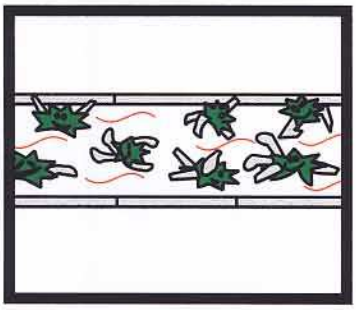
Several days later and Beccy starts to experience flu-like symptoms and memory loss.



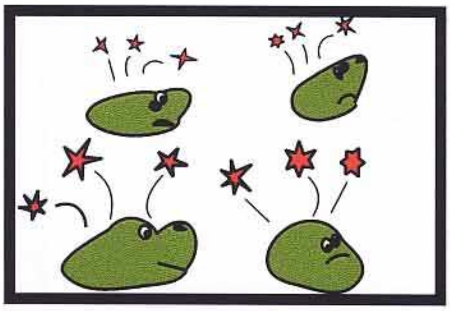
Staphylococcal bacteria living on her tampon, are releasing toxins, which attach directly onto the 'attack' proteins.

A violent reaction starts, but unlike food, the tampon cannot be expelled. Things deteriorate as toxins continue to be produced.

<u>**SEPTIC SHOCK**</u>



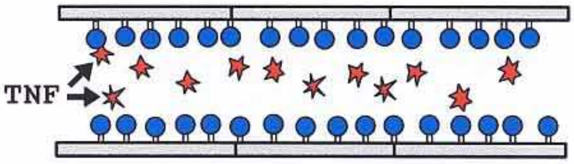
These gram - negative bacteria have infected someone's blood.



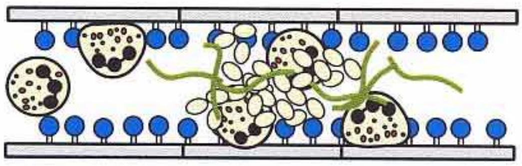
Endotoxins from the bacteria, then trigger macrophages into releasing tumour necrosis factor.

Without prompt medical intervention, things could rapidly deteriorate.

High levels of TNF, relax arterial tone all over the body. This can depress heart and brain function.



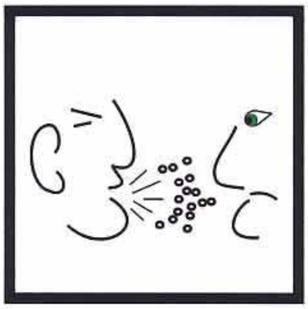
High levels of TNF also cause endothelial cells lining the blood vessels to express surface markers.



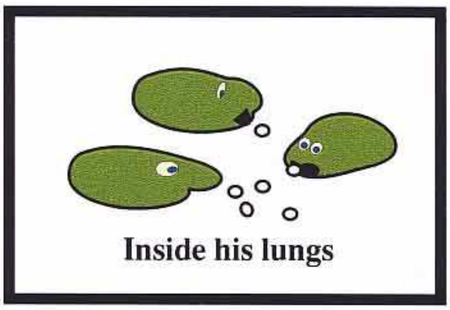
Platelets, neutrophils and fibrin now attach onto the surface markers and could block small blood vessels.

MYCOBACTERIUM TUBERCULOSIS (TB)

This gram-positive bacillus, replicates slowly and has a tough, protective, waxy exterior.



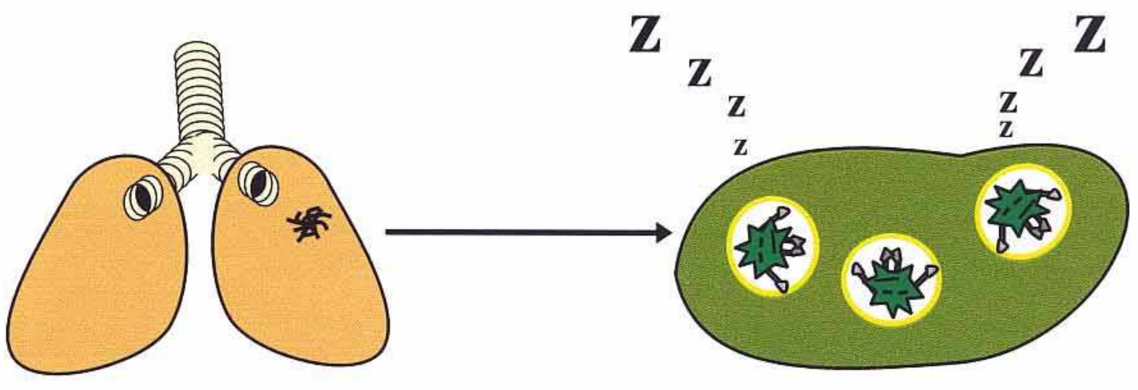
Infected droplets are inhaled from someone with active TB.



Macrophages 'gobble' up the bacilli, but their waxy exterior stops them from being 'digested'.

But once a T helper releases its stimulating cytokines, the bacilli are finally killed off.

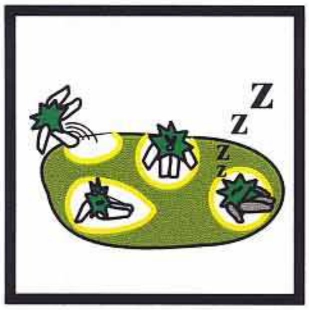
So without sufficient T helper stimulation, the bacilli can survive inside the macrophage.



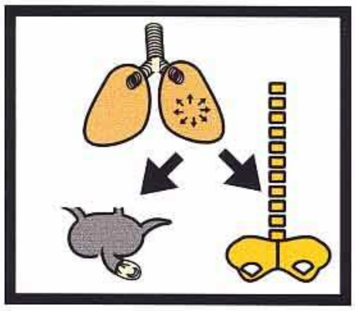
A calcified lesion may appear, following the primary infection.

Unfortunately, this lesion sometimes conceals a nasty secret. Dormant spores!!!

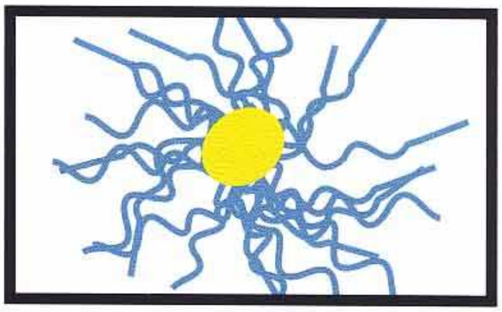
MONTHS LATER AND A PERIOD OF ILL HEALTH



The spores reactivate, now conditions have 'improved' for them!!



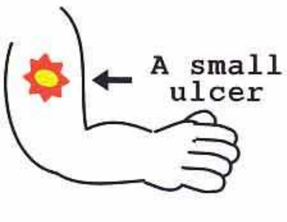
Soon tuberculosis lesions start to appear at other sites in the body.



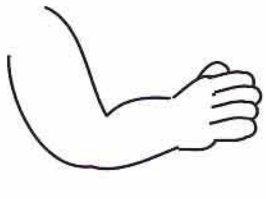
A typical tuberculosis lesion has a 'cheesy' centre and surrounding fibrous tissue, containing activated macrophages and T helper cells.

THE HEAF TEST SHOWS IF YOU ARE PROTECTED AGAINST TUBERCULOSIS

Killed tuberculosis bacilli are injected.



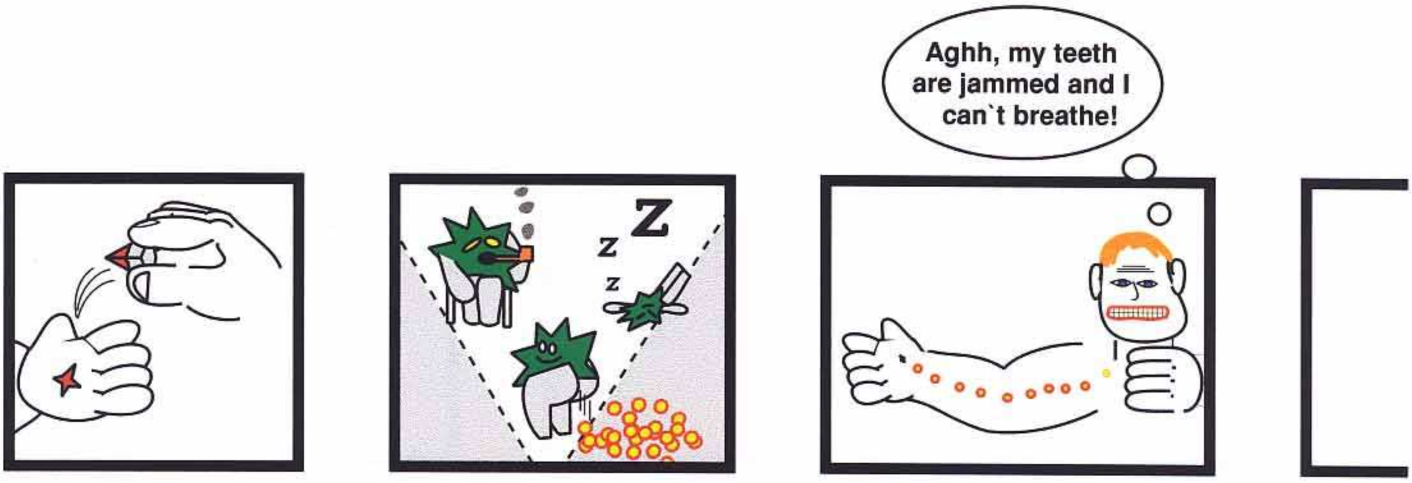
A good / positive tuberculin reaction.



A bad / negative tuberculin reaction.

A negative reaction, shows there are insufficient numbers of anti-TB T helper cells and immunisation against TB is advisable.

TETANUS

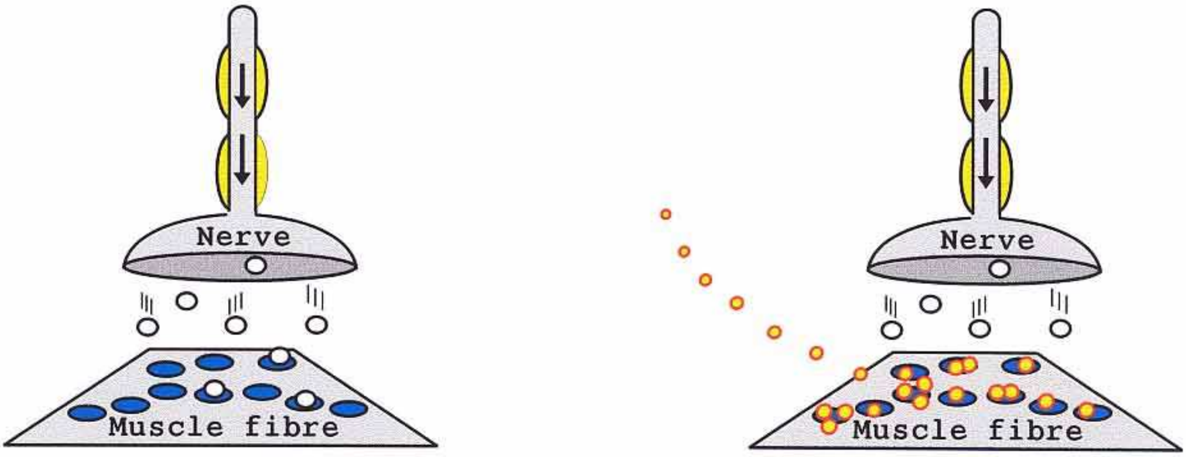


Just another garden injury, or is it?

The bacteria, clostridium tetani, now lodge under the skin.

Soon they start to release waste (exotoxins), which could be fatal!!!

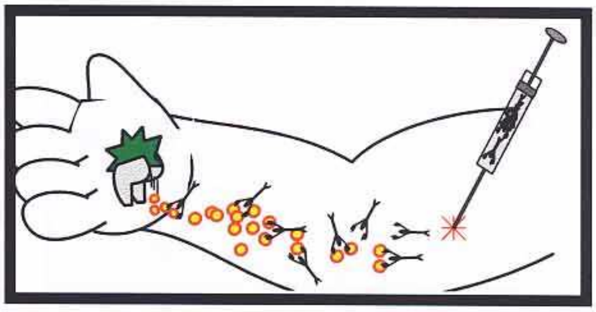
HOW TETANUS TOXINS STOP MUSCLES WORKING




```
Normally, nerve impulses reaching
the end of a nerve, trigger
acetylcholine to be released onto
a muscle, causing it to contract.
```

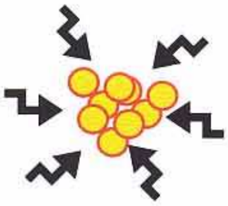
```
Tetanus toxins attach onto the
acetylcholine receptors, so
that nerve impulses cannot
reach and stimulate the muscle.
```

The nurse injects antibodies with 'hands', that fit the tetanus toxins.

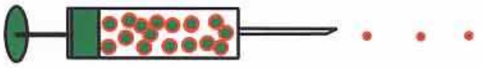


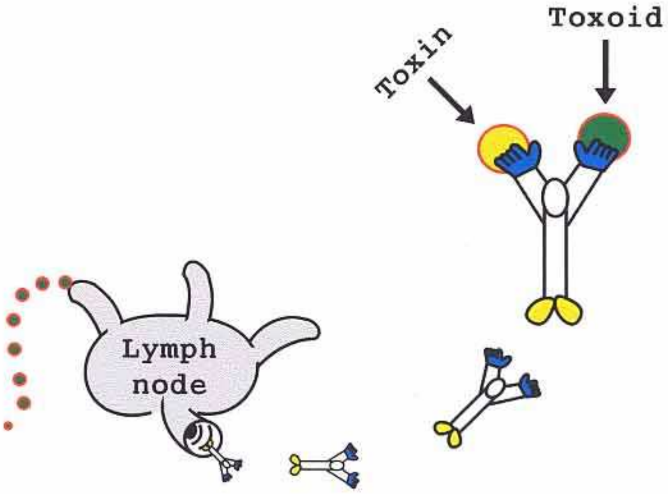
They 'grab' the toxins, but as these antibodies are not made by the patient, they will soon disappear.

THE PERMANENT SOLUTION



Tetanus toxins are treated so that they become harmless, but their shape is unaltered.

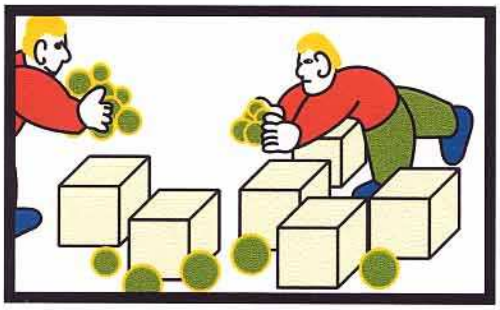




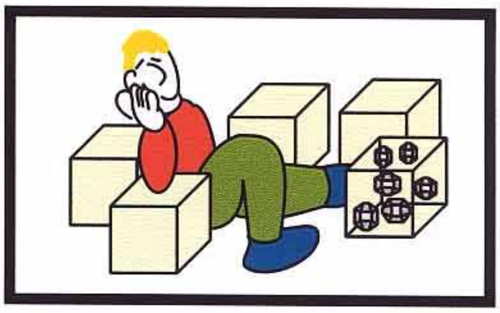
The harmless toxins, now called "tetanus toxoid", is injected.

2 weeks later, IgG with 'hands' that fit both toxin and toxoid molecules, start to appear.

VIRUSES



Most bacteria live in the 'open' and can be 'eaten up' by macrophages.

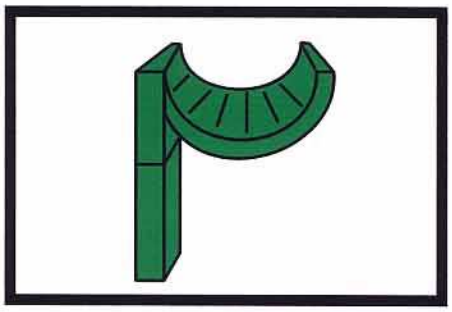


But viruses live inside living cells, 'well hidden' from macrophages.

So for the immune system to fight viruses, it is a whole new ball game!

CHAPTER FOUR

THE 'DEFENCE' PROTEIN

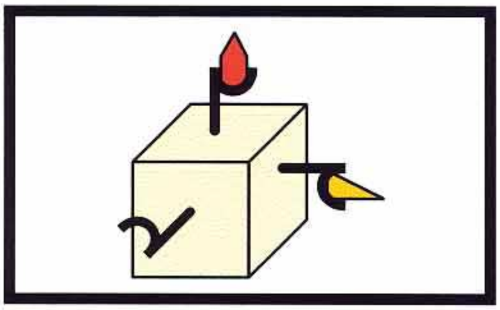


The 'defence' protein is found on the surface of every nucleated cell in the body.

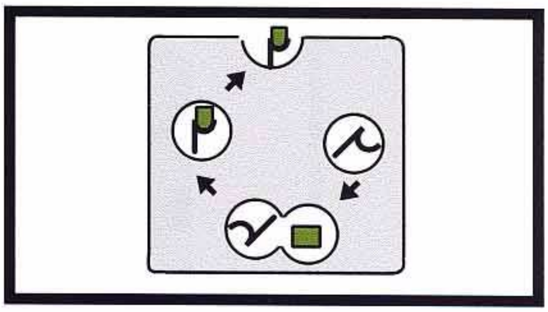
Easy reading

Technical information

The 'defence' protein's technical (offical) name, is the major histocompatibility complex (MHC) class 1 protein.



The cleft at the top of the 'defence' protein, often holds small lengths of protein from inside the cell.

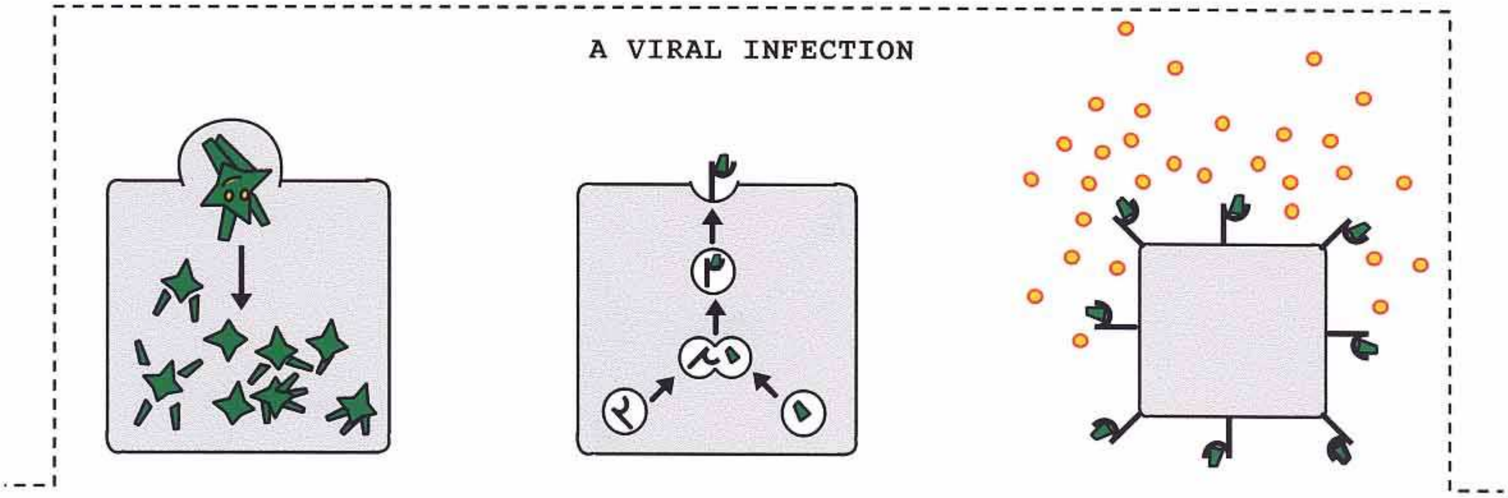


These are 'picked up', as the 'defence' proteins continually circulate between the surface and the interior.

The cleft can hold small lengths of protein, about 10 amino acids long.

NOW MEET T CYTOTOXIC LYMPHOCYTE

His beat is in the blood.

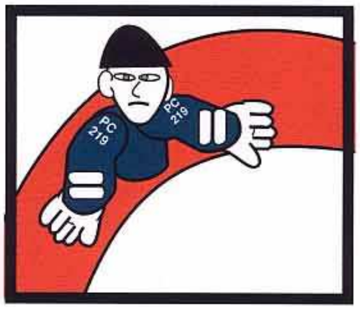


If a virus can get into a cell, it will start to replicate itself.

Viral proteins soon appear at the cell's surface, attached to 'defence' proteins.

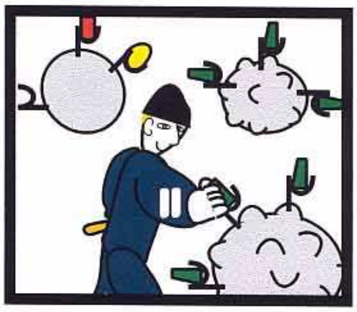
Infected cells will also release alpha interferon to 'warn' other cells (see page 295).

AT THE SITE OF THE INFECTION

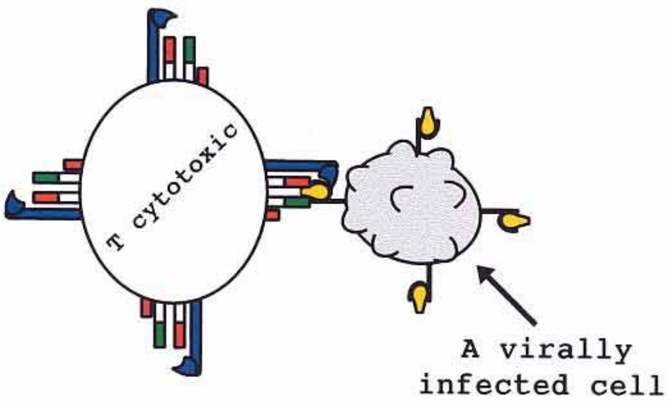


T cytotoxic cell appears from a blood vessel, close to the infection.

But a nearby macrophage is completely oblivious to the 'hidden' danger.

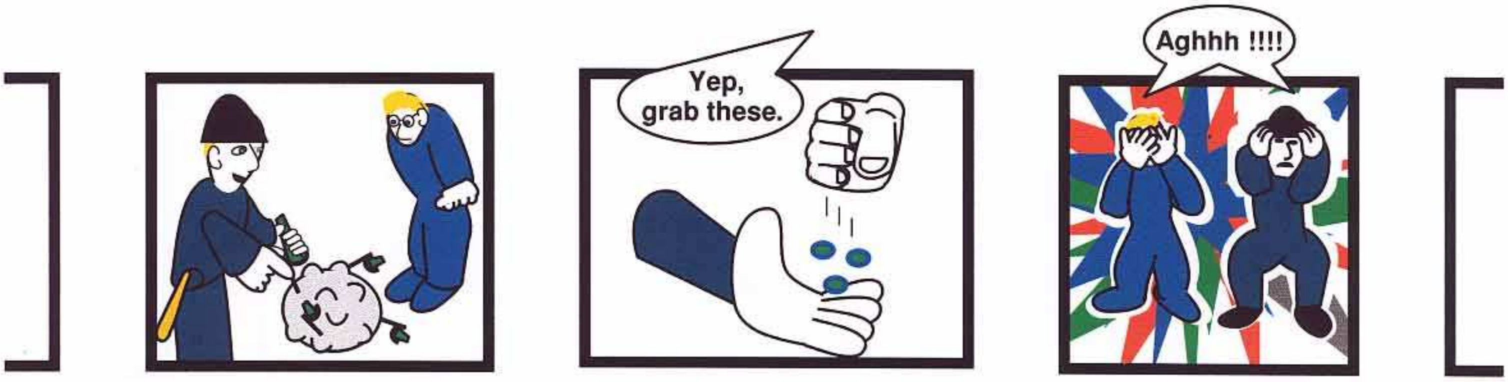


However, it is not long before he starts to find the virally infected cells.



T cytotoxic cells have surface receptors which act like 'hands'.

T HELPER TURNS UP TO SEE IF HE CAN HELP

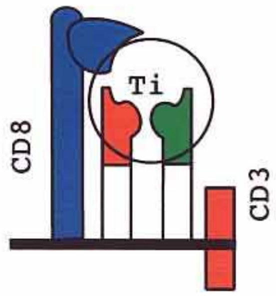


T cytotoxic shows this T helper an infected cell.

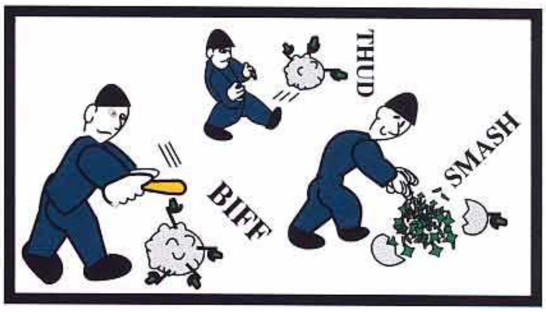
Satisfied that it is infected, T helper releases cytokines like interleukin-2.

Both cells now start to feel very strange!

2 T CYTOTOXIC CELL 'HAND' SHAPES



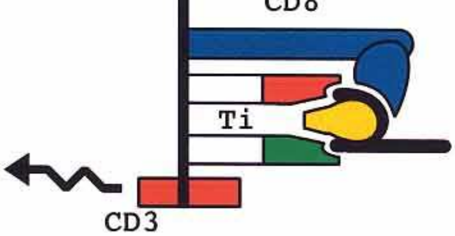
Although all T cytotoxic cells have 'hands' (ie CD3, CD8 and Ti molecules), each has a unique shape at the end of their Ti molecule. It is this which greatly restricts what will fit into its 'hand'.



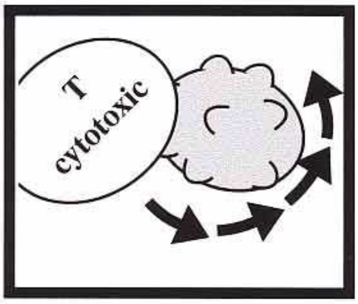
Clones, identical copies of the original T cells, start appearing.

The cytokines from the T helper cell, also triggers the T cytotoxic cells into attacking the virally infected cells.

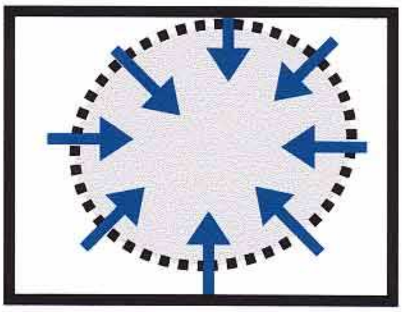
FOR THAT PERFECT FIT



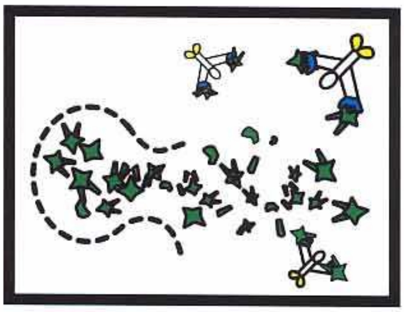
1. CD8 attaches to the side of the 'defence' protein.
2. Ti fits over the top of the 'defence' protein + viral protein.
3. CD3 can now signal to the nucleus that the 'hand' fits.



Moving around its victim, perforin is discharged onto its surface.



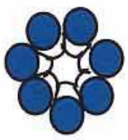
The perforin punctures the membrane, allowing water to flow into the infected cell.



The cell swells and bursts, releasing the 'hidden' viruses for antibodies to eliminate.

The T cytotoxic cell also releases toxins into the target cell, which will disrupt its nucleus.

Side view



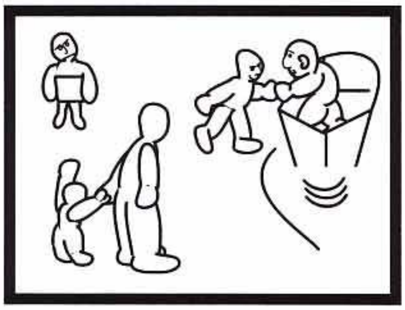
Top view

A perforin complex is round, with a hole through the centre. It is very similar to a membrane attack complex (see page 270).

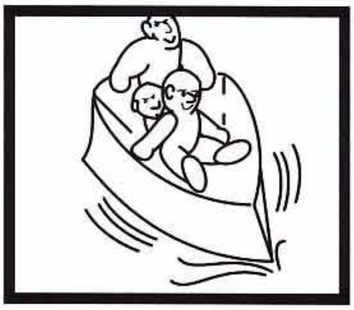
CHAPTER FIVE

THE THYMUS GLAND

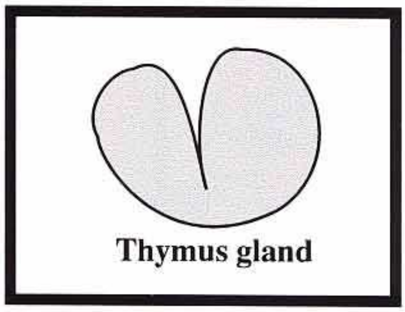
BABY T CELLS GROW UP IN THE THYMUS GLAND



To mature, all baby T cells must leave the bone marrow for the thymus gland.



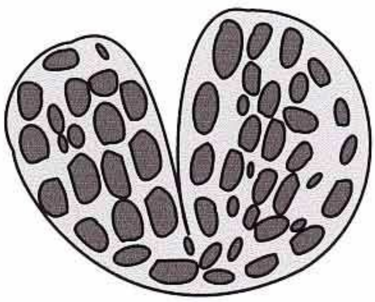
To get there, they travel via the blood.



Maturation then occurs in one of the thymus gland's many lobules.

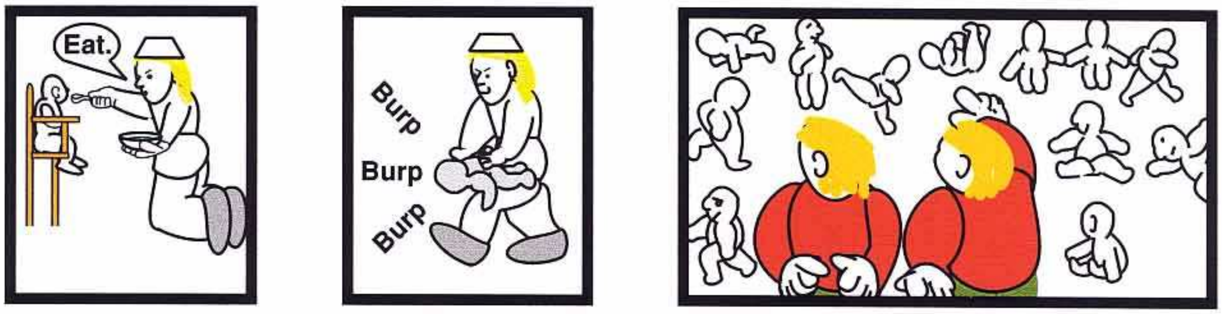
Easy reading

Technical information

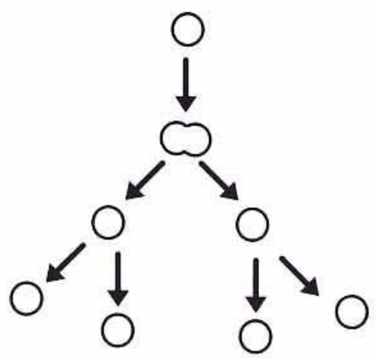


The thymus is made up of many lobules.

Each lobule has an inner medulla and an outer cortex.

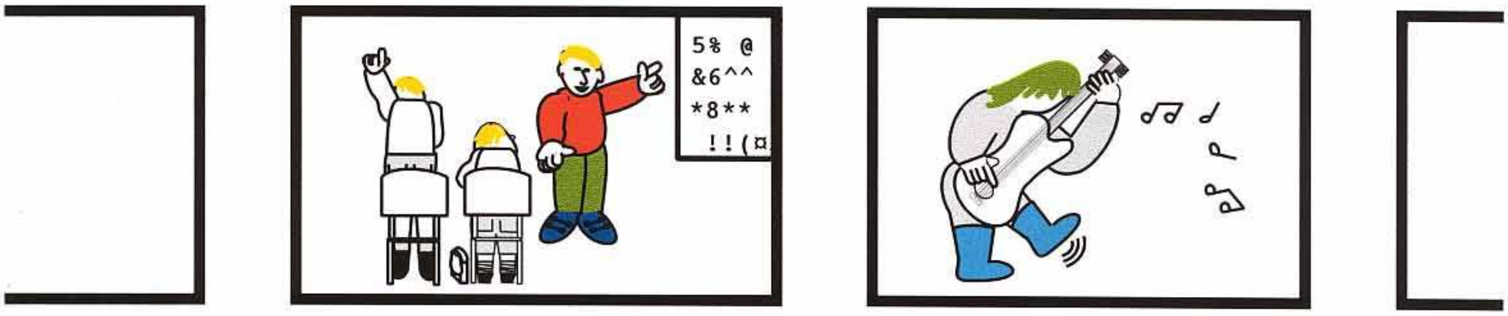


Resident nurse cells and macrophages, encourage the young T cells to grow and develop.



Before a young T cell matures,
it will first replicate itself.

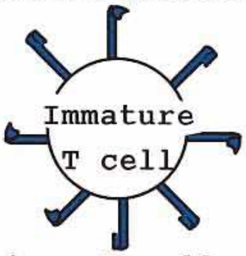
THYMIC EDUCATION



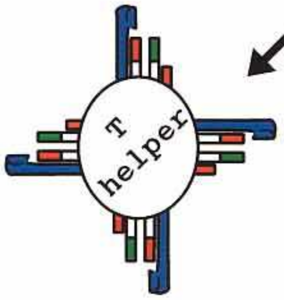
The time spent in the thymus by a T cell, is called "thymic education".

Any T cell which fails to fully develop, is killed off.

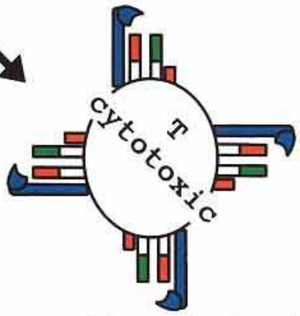
POSITIVE SELECTION



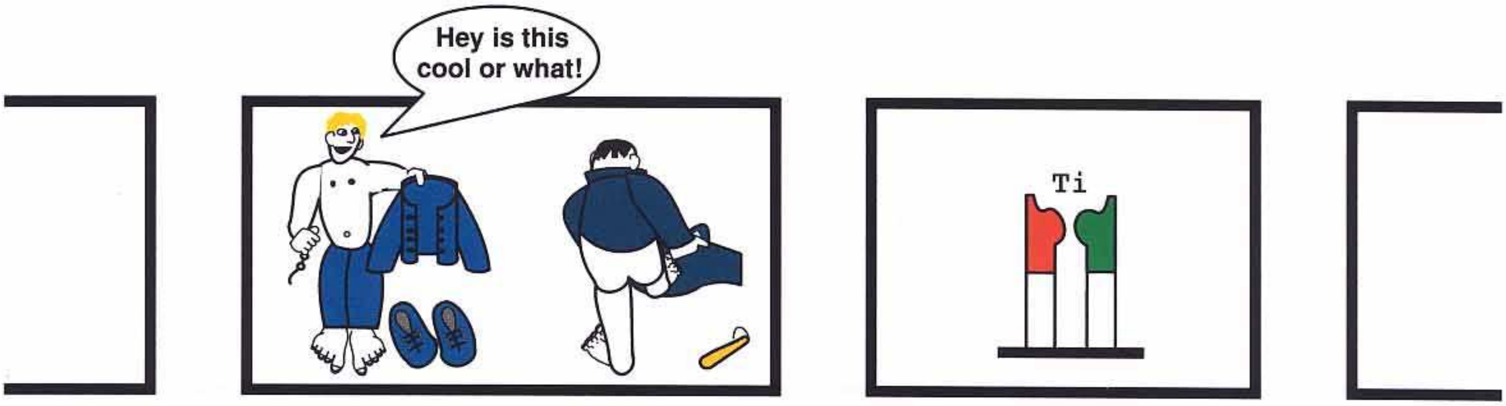
The immature T cell expresses both CD4 and CD8 molecules.



A mature T helper loses its CD8 molecules, but gains CD3 and Ti molecules.



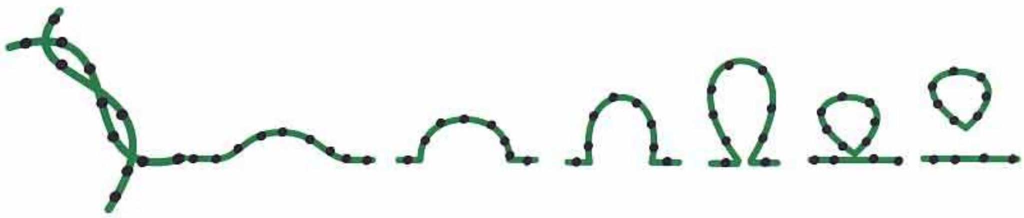
A mature T cytotoxic cell loses its CD4 molecules, but gains CD3 and Ti molecules.



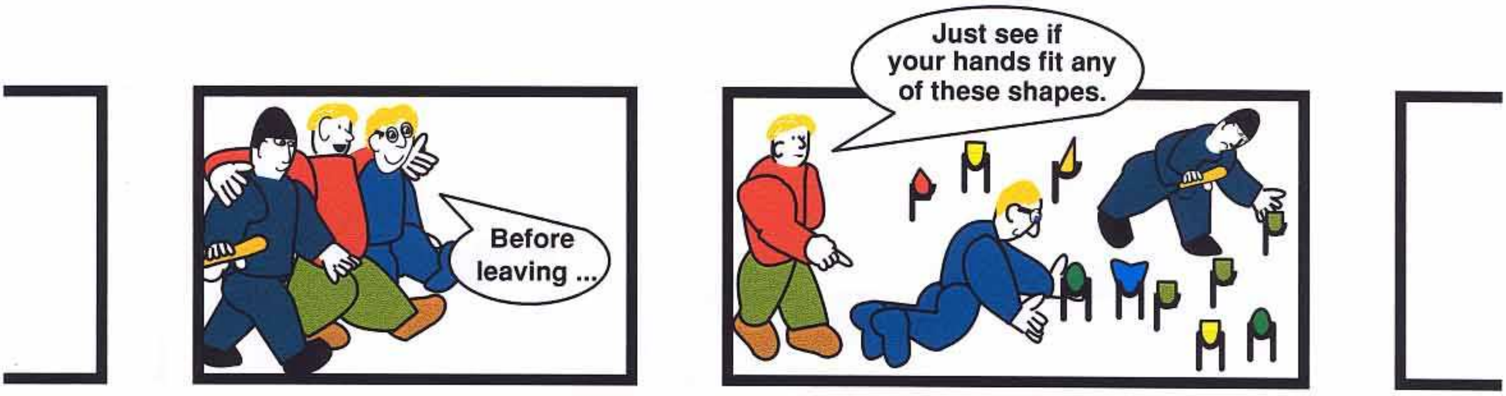
As each T cell develops into either a T helper or a T cytotoxic cell, it also acquires a unique fixed 'hand' shape.

The mature T cell's unique 'hand' shape was featured on pages 84 and 114.

INSIDE THE IMMATURE T CELL



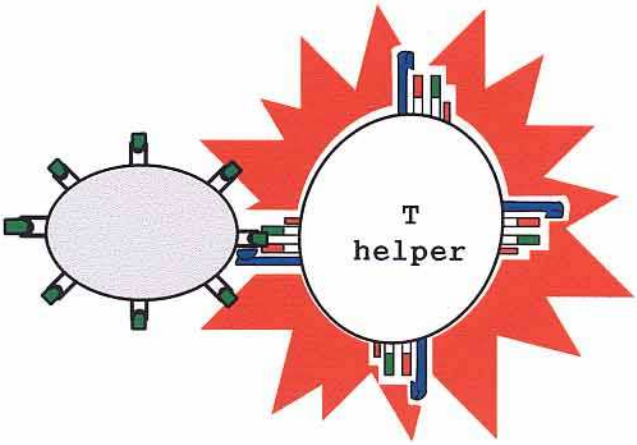
Genes coding for an immature T cell's 'hand' shape, undergo random gene rearrangement (ie small lengths of DNA are removed). So although there are millions of T cells, each has a unique fixed 'hand' (Ti) shape.



But before a mature T cell can leave the thymus gland, it must undergo negative selection.

95% OF ALL T CELLS IN THE THYMUS WILL DIE

NEGATIVE SELECTION



Once they are fully developed, T cells are exposed to 'attack' and 'defence' proteins, holding pieces of protein belonging to the host. If their 'hands' fit, like the T helper above, they will die.

T cells whose 'hands' do not fit anything, leave the cortex and enter the lobule's medulla.

From the medulla, they will pass out into the blood, to start their life's work.

The T cell receptor must only be able to attach onto:-

Foreign protein + 'attack' protein (see page 85).
OR
Foreign protein + 'defence' protein (see page 115).

T helper lymphocytes are sometimes called "CD4" or "T4" cells.

T cytotoxic lymphocytes can be referred to as "CD8" or "T8" cells.

Both these cells will now live for years.

Lymphocytes have a large nucleus.

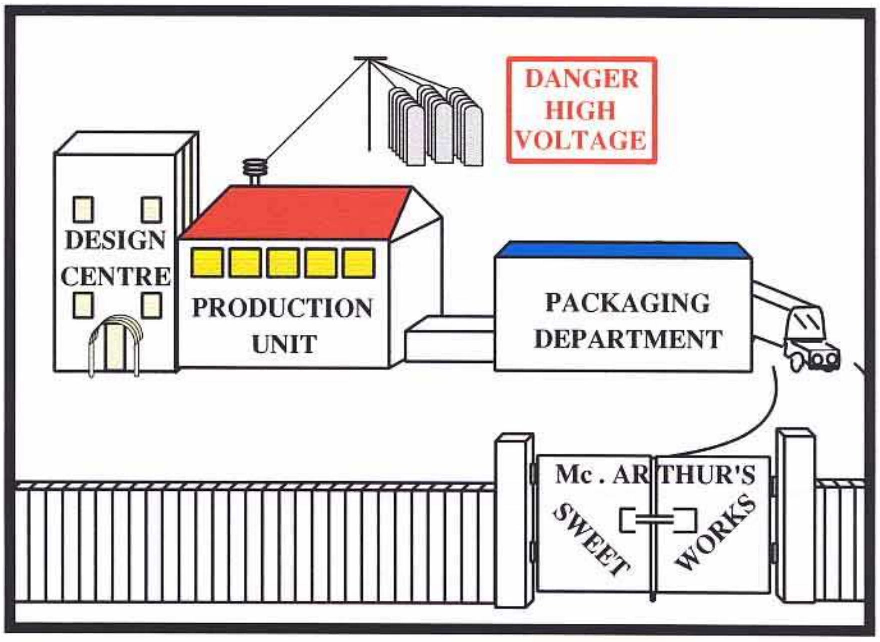
B lymphocytes are so called, because they were first discovered in the bursa of Fabricus, in birds.

T lymphocytes must mature in the thymus gland, hence they acquired the title of T cells.

CHAPTER SIX

UNDERSTANDING VIRUSES

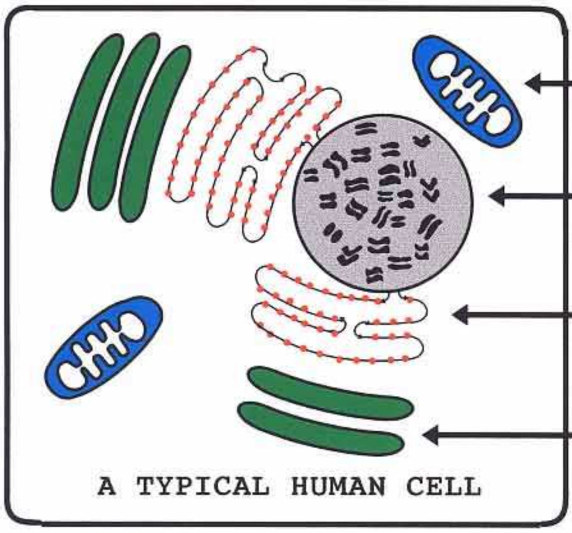
THE WORKINGS OF A NORMAL CELL



A cell is similar to a factory complex, where separate areas work together to produce a finished product.

Easy reading

Technical information

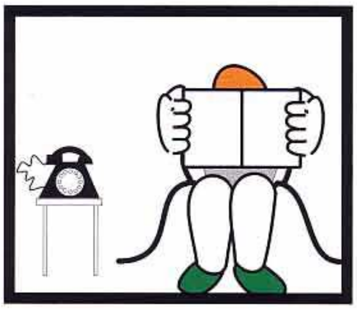


A mitochondria generates energy to power the cell.

The nucleus with its chromosomes, is the cell's 'design centre'.

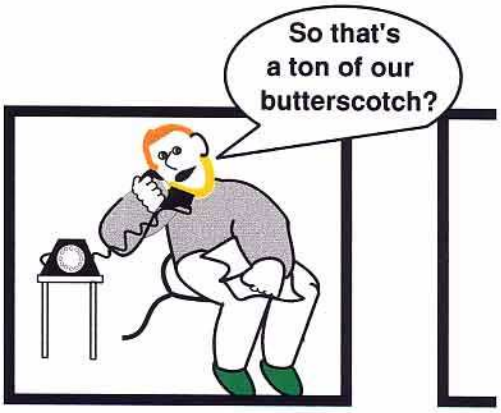
The rough endoplasmic reticulum does all the 'production' work.

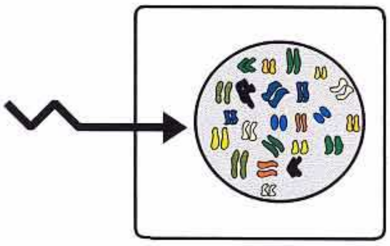
The golgi apparatus must then 'package' the finished product before it can leave the cell.



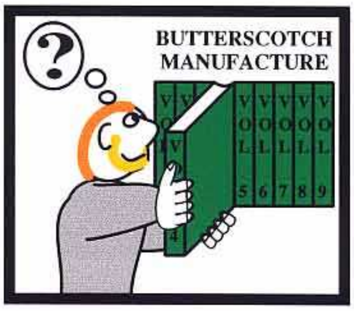
Nick, an enzyme in the nucleus, was reading his morning paper.

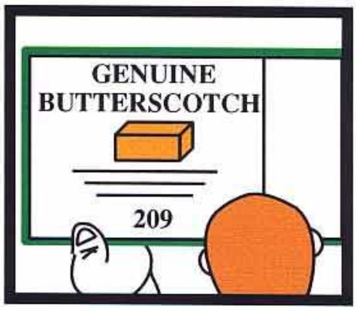
But he didn't have to wait long for the first order of the day to arrive.





This cell receives a message (eg a hormone), which triggers it into making a particular product.

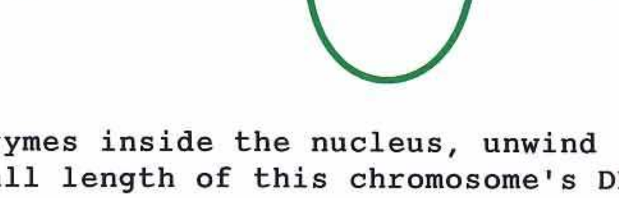




After receiving the phone call, Nick goes to the far end of his office where all the reference books are kept.

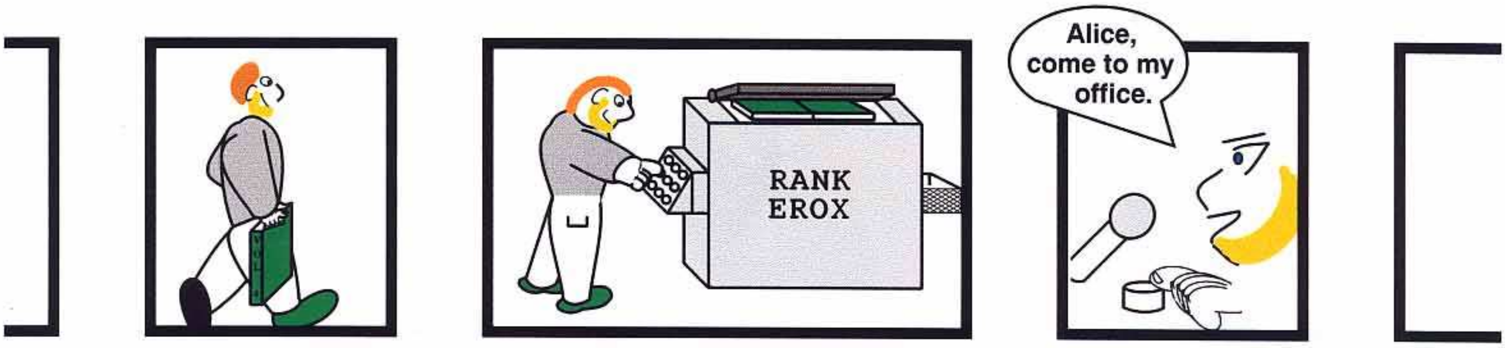
He now turns to the appropriate page.

GAINING ACCESS TO INFORMATION ON A CHROMOSOME



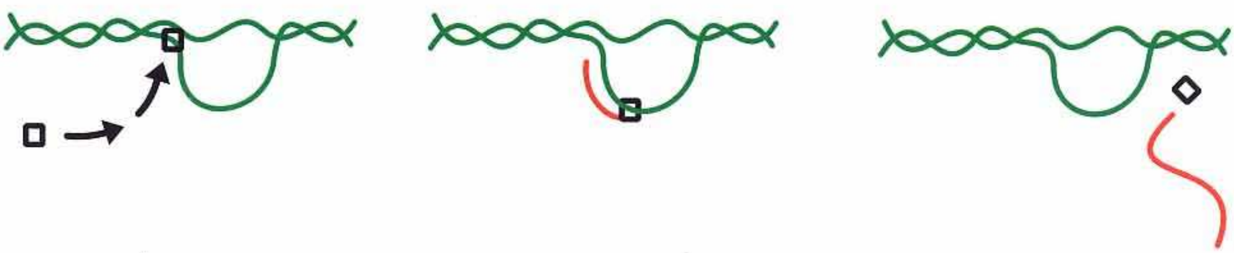
DNA

Enzymes inside the nucleus, unwind a small length of this chromosome's DNA.



As the reference books are too valuable to be taken out of his office and onto the shop floor, Nick photocopies the recipe.

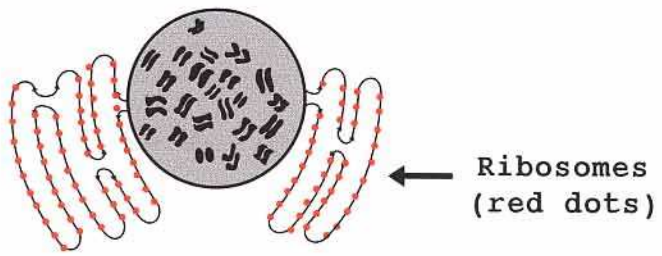
TRANSCRIPTION



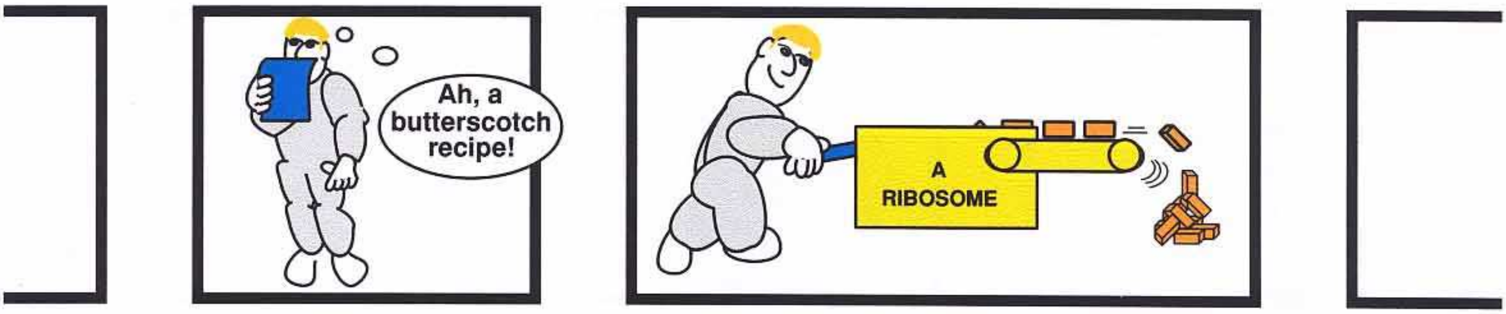
RNA polymerase now attaches onto the exposed DNA.

Moving along the DNA, a copy (messenger RNA), is produced.

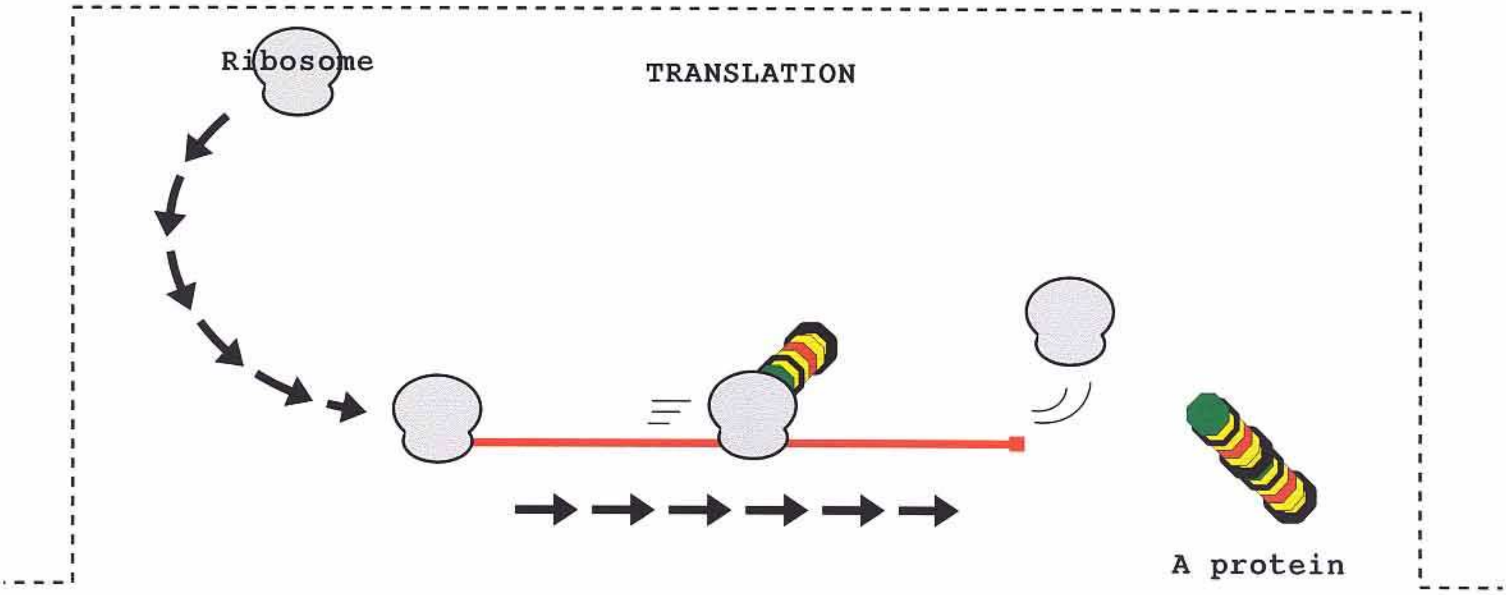
Alice takes the photocopied recipe and leaves the design centre for the production unit.



The messenger RNA is transported out of the nucleus and into the rough endoplasmic reticulum.



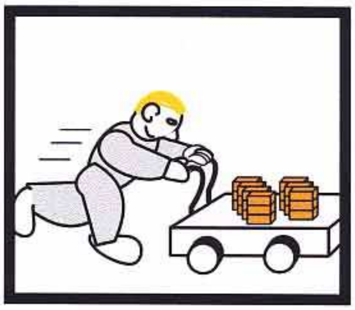
Frankie, one of the workers on the shop floor, inserts the recipe into a ribosome and butter-scotch production begins.



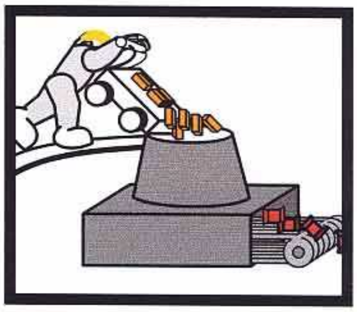
A ribosome attaches onto the mesenger RNA. Then as it moves along the RNA, protein synthesis begins.

Reaching the end of the RNA, the protein detaches and the ribosome returns to start another 'run' along the RNA.

Kieth, one of the other workers, now gathers up the butterscotch.

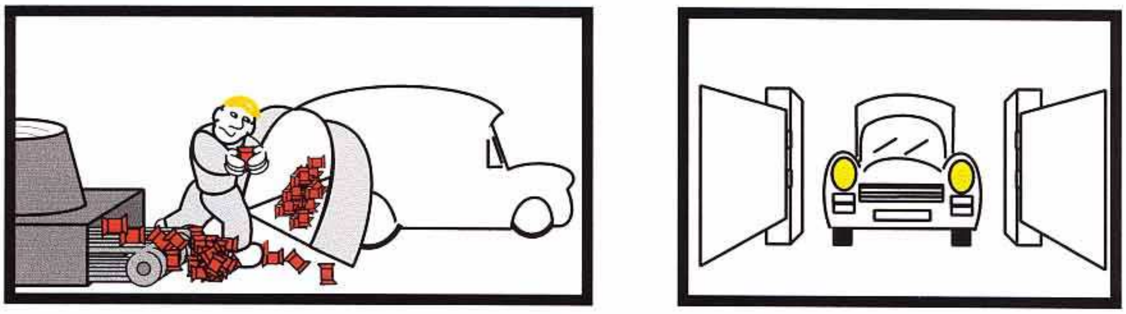


He then quickly speeds off to the factory's packaging department.



Soon things are wrapped up!!!.

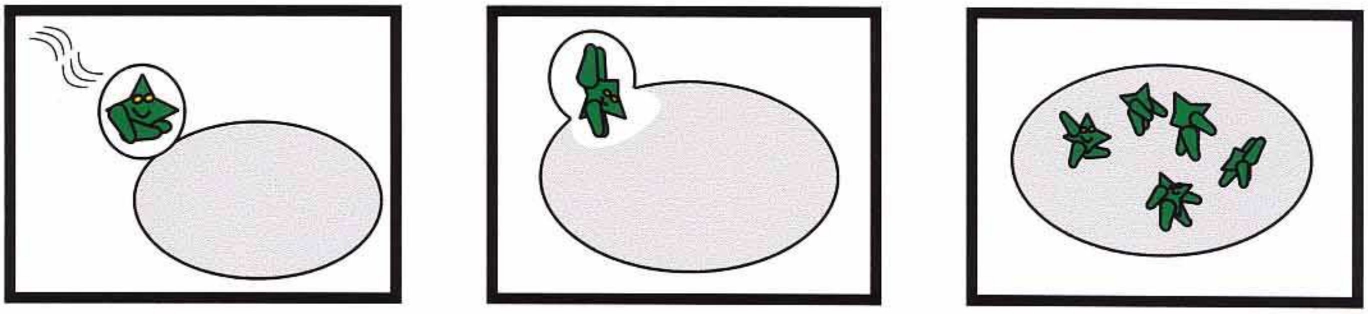
The protein is now transported to the golgi apparatus for 'packaging'.



After being wrapped, the sweets are loaded into a van and are soon on their way.

```
Once 'packaged', the protein is released
from the cell into the blood, so it  can
be utilised by another part of the  body.
```

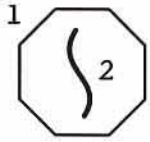
TO SURVIVE AND REPLICATE, A VIRUS MUST ENTER A LIVING CELL



A virus contacts the outer surface of this target cell.

The 2 membranes fuse, allowing viral material to flow into the target cell.

Viral replication can now start inside the cell.

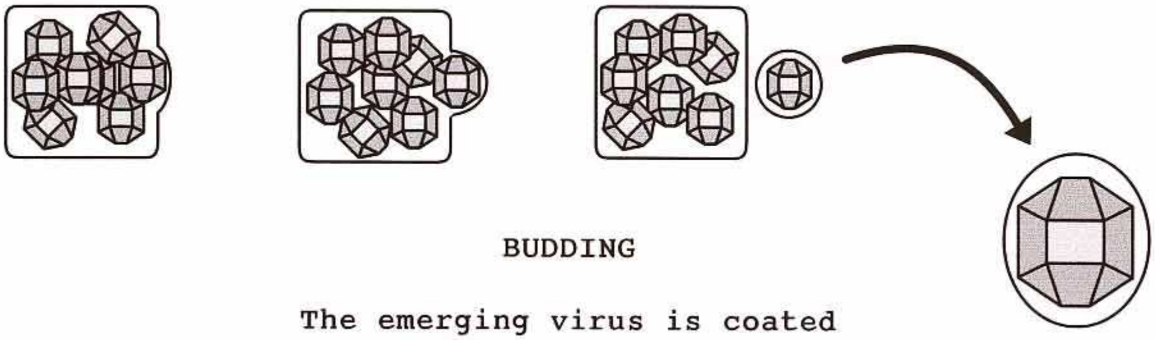


A VIRUS

A virus is little more than a protein coat called a "capsid" (1), protecting a small amount of genetic material (2).

THE 2 WAYS A VIRUS CAN LEAVE A HOST CELL

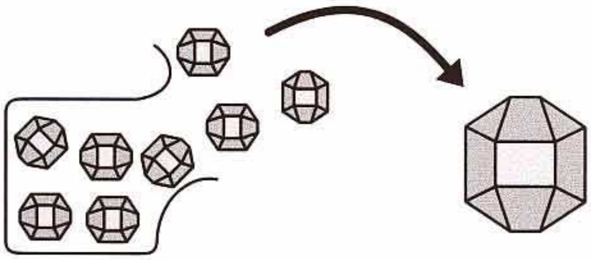
1



BUDDING

The emerging virus is coated in the host cell's membrane.

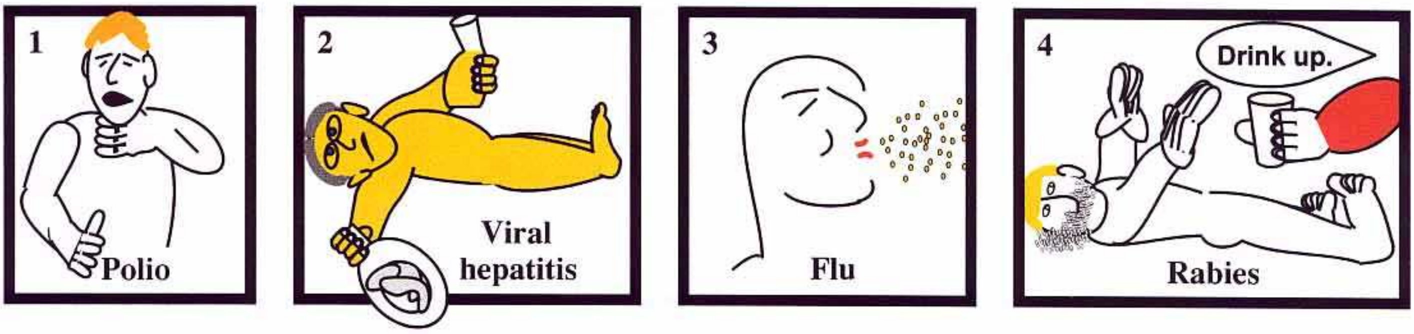
2



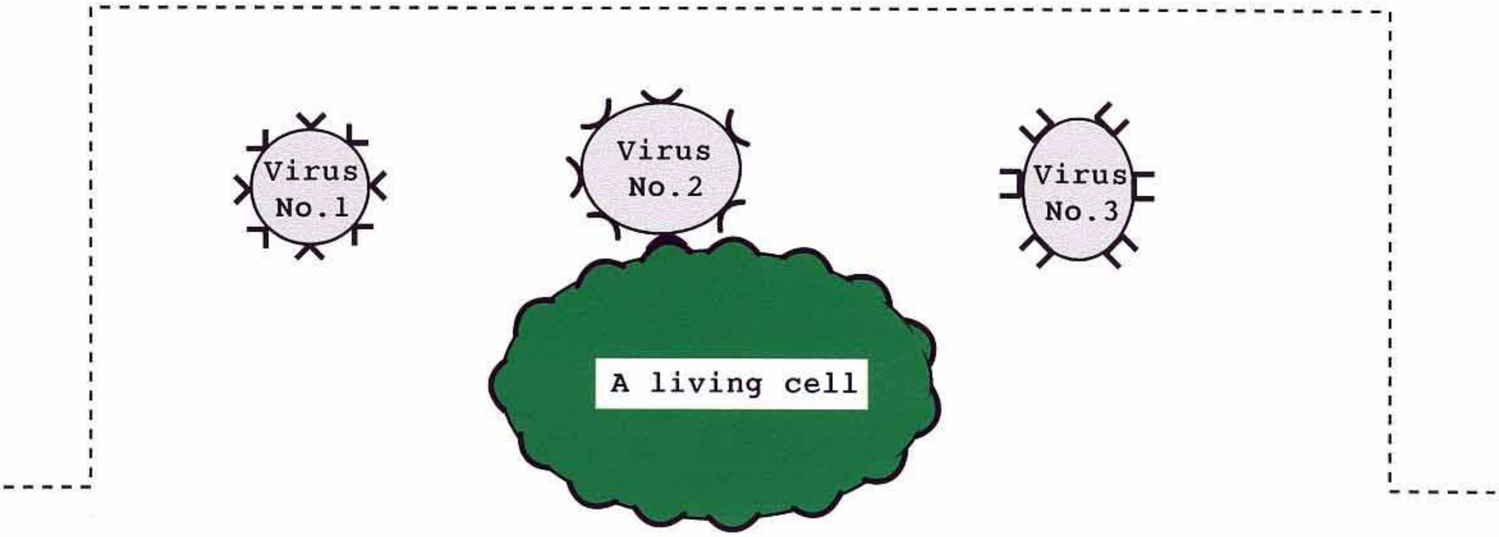
LYSIS

The infected cell bursts and this releases nude viral particles.

4 VIRAL INFECTIONS

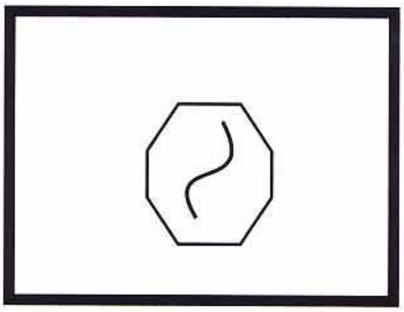


Each of these viral infections results in the appearance of very specific signs and symptoms. This is simply due to the fact that a virus is very limited in the cells it can infect (penetrate).

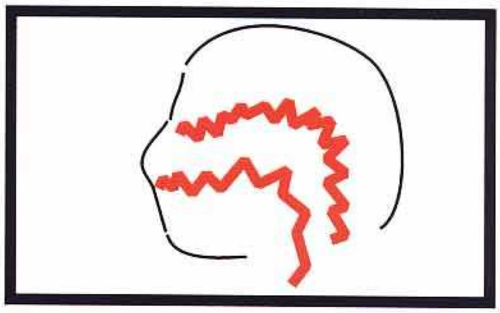


Before a virus can enter and infect a cell, it must have the right shaped surface receptors, to be able to attach onto the target cell's membrane.

THE COMMON COLD / RHINOVIRUS

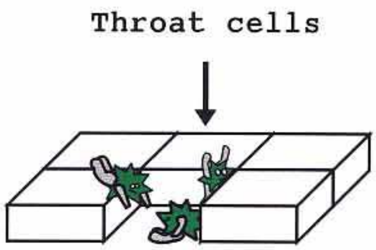


The rhinovirus contains a single strand of viral RNA.

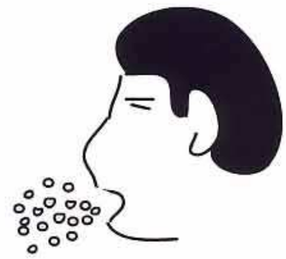


It infects cells lining the upper respiratory tract. The resulting inflammation and oedema produces a dry cough and runny nose.

The rhinovirus remains fairly localised, as it can only function at around 33°C and the body's core temperature is 37°C.



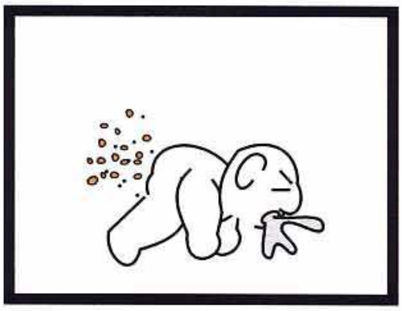
Damage caused by this virus can sometimes allow opportunistic bacteria to 'move in'.



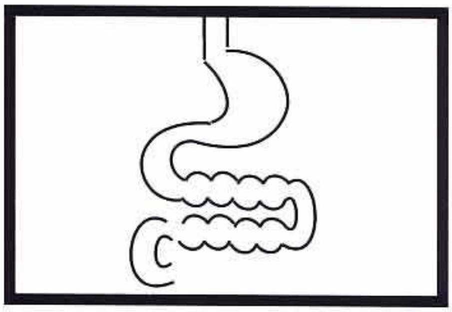
Now sputum starts to be expectorated and it is time for antibiotics.

THE ROTAVIRUS

The rotavirus is a double - stranded RNA virus.



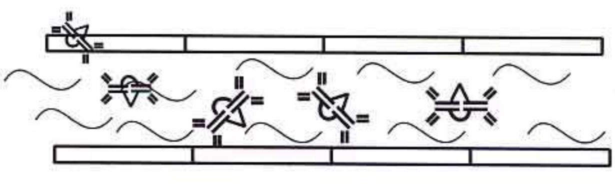
It mostly affects 6 to 24 month old babies, causing diarrhoea and vomiting.



The virus infects the lining of the small intestine, causing its microvilli to become flattened.

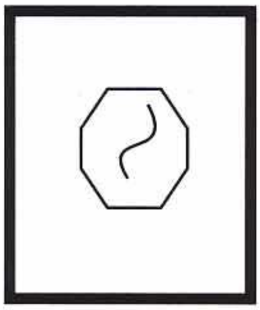
To help avoid this infection, it is important to wash your hands before feeding a baby.

POST INFECTION / IMMUNITY

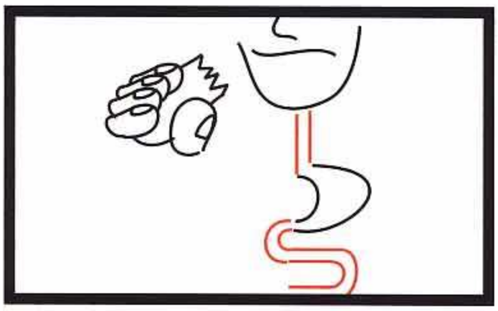


Following a rotavirus infection, IgA with 'hands' which fit this virus, are released into the gut.

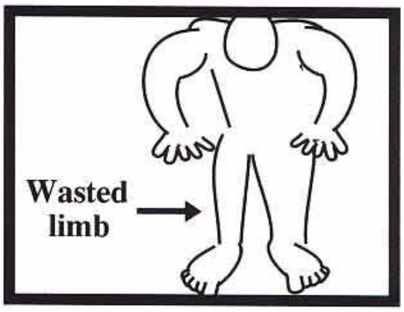
POLIOMYELITIS



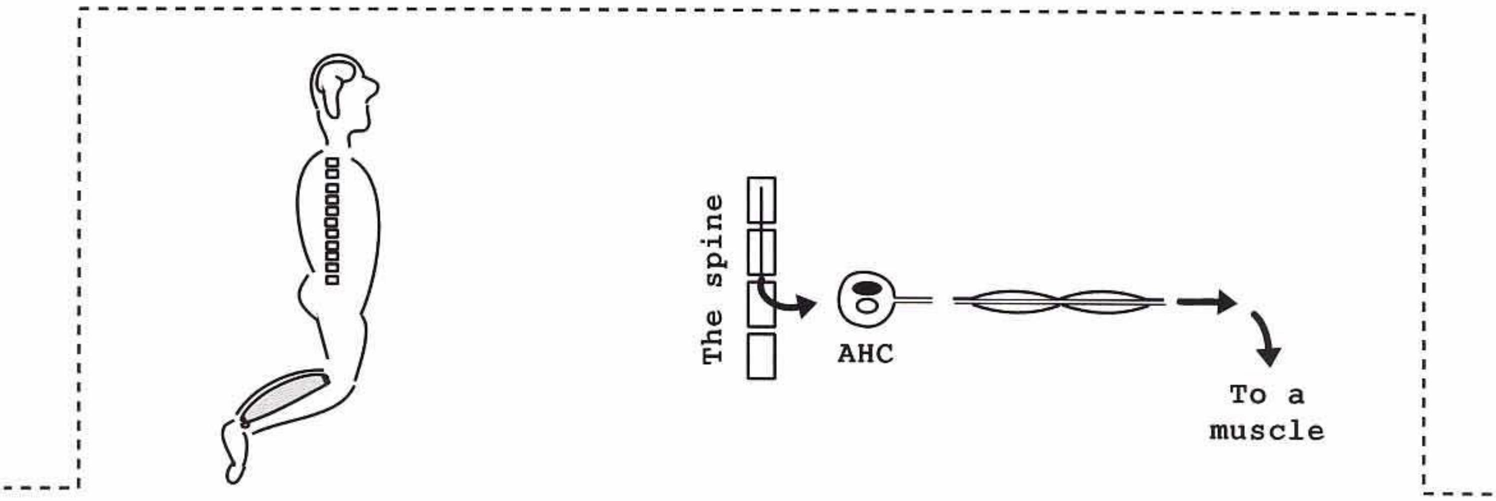
The poliovirus has a single strand of RNA.



The virus usually only infects the throat and intestines, producing mild symptoms (ie a sore throat).



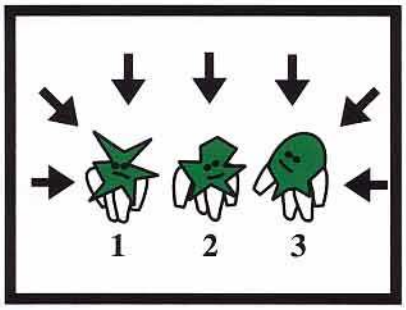
But in a few cases, the virus then reaches the spine and paralysis can now occur.



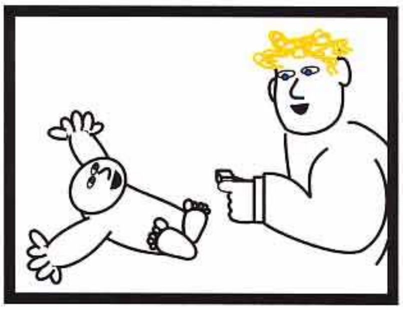
To move your foot, nerve impulses must pass from the brain, down the spine and out through the anterior horn cells (AHC's), to the muscles. The poliovirus can infect and destroy one or more AHC's which could prevent nerve impulses reaching the muscles and so lead to paralysis.

POLIO IMMUNISATION

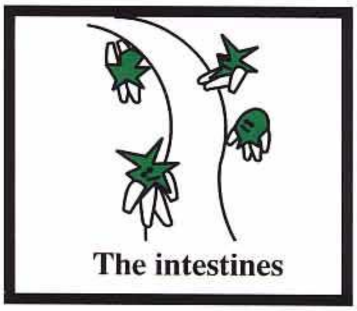
There are actually 3 closely related polioviruses.



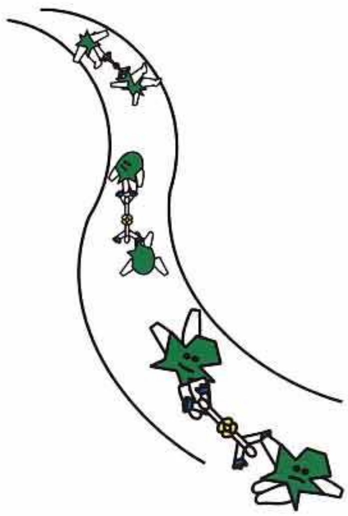
The 3 viruses are repeatedly breed (attenuated), so they remain localised in the gut.



The live (attenuated) vaccine is now given to a baby, some-times on a sugar lump.



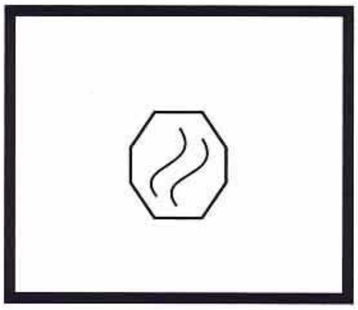
The treated viruses start to replicate in the gut.



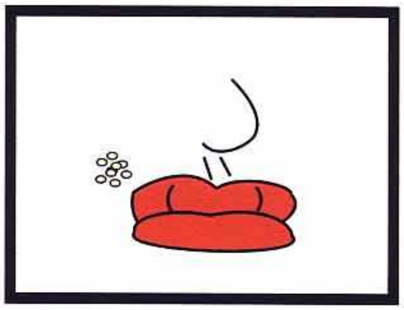
IMMUNITY (see page 48)

2 weeks later, anti - polio IgA are released into the gut. These attach onto the polioviruses so that they are flushed away. Anti-polio antibody production, will now continue for many years.

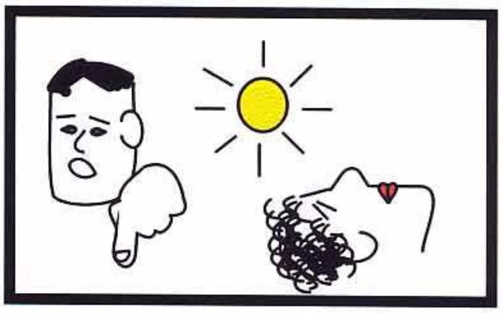
HERPES SIMPLEX



The herpes simplex virus is a double - stranded DNA virus.



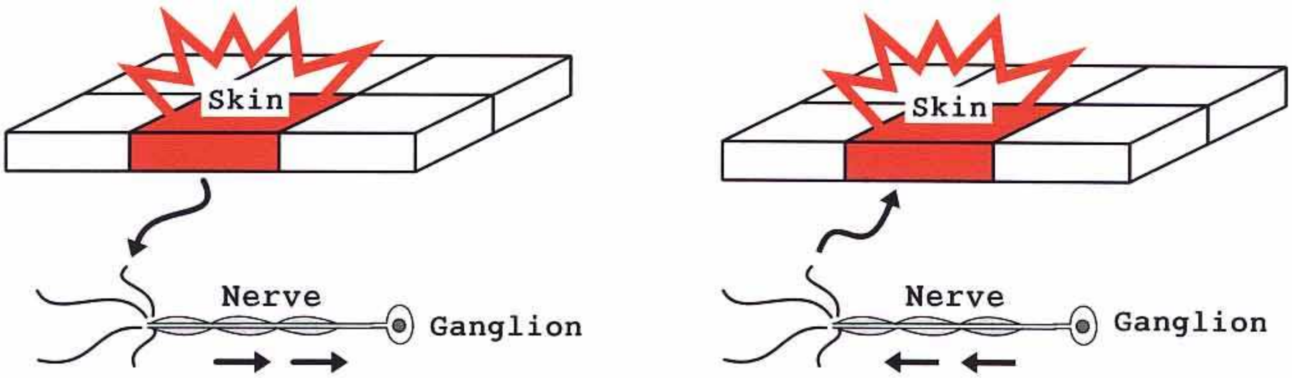
It causes painful blisters to erupt onto the skin, which then last a few days.



Weeks / months later, factors such as fear or sunlight can reactivate the virus and the cycle repeats itself.

Close contact with other people must be avoided, whilst the virus is active.

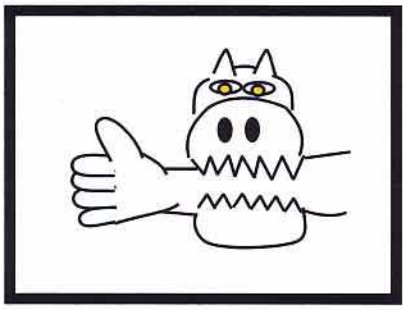
SO WHY DOES THIS SKIN LESION PERIODICALLY REAPPEAR?



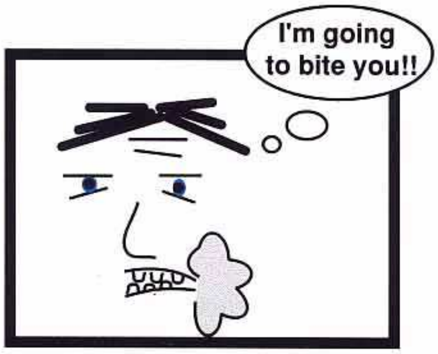
After infecting skin cells, the virus migrates along a sensory nerve to infect its ganglion. The infected skin cells are eliminated but not the infected nerve ganglion. Then at a later date, the virus reactivates and migrates back along the nerve, to reinfect skin cells.

RABIES

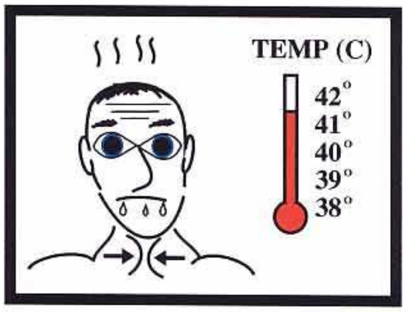
A single strand, RNA virus.



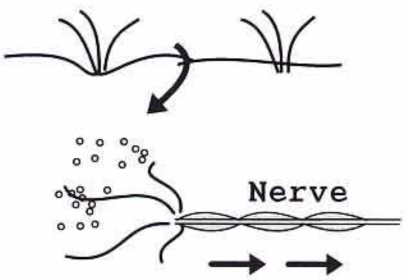
Rabies can be contracted if a bite from an infected animal, happens to puncture the victim's skin.



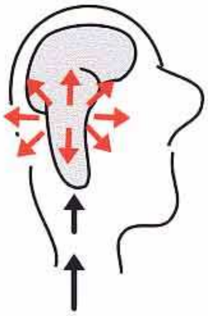
The virus will now target cells in the brain and the salivary glands.



Symptoms include:- dilated pupils, excessive salivation, fever, anxiety, hydrophobia and a desire to bite!!!

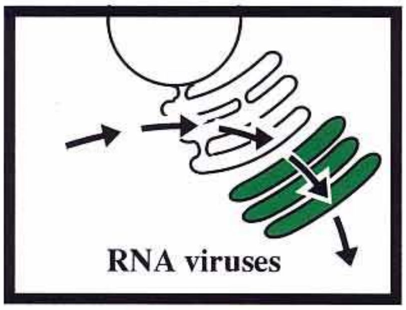


The rabies virus replicates under the skin, before tracking back along a nerve to the brain.

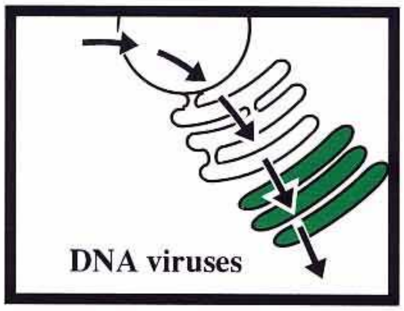


In the brain, the thalamus, hypothalamus and pons are all infected by this virus.

HOW VIRUSES USE OUR CELLS



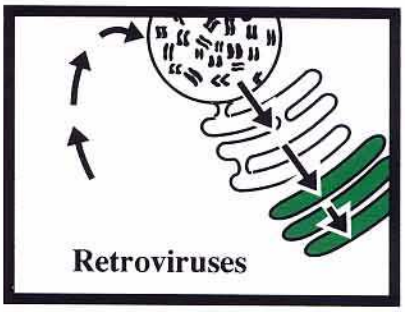
Viral RNA goes straight to the ribosomes and viral replication begins.



Viral DNA enters the cell's nucleus and is transcribed into viral RNA.

↓

The viral RNA is then transported out to the ribosomes and viral replication begins.



Viral RNA enters the cell and is transcribed into viral DNA.

↓

The viral DNA is then transported into the nucleus and incorporated onto one of the host's chromosomes.

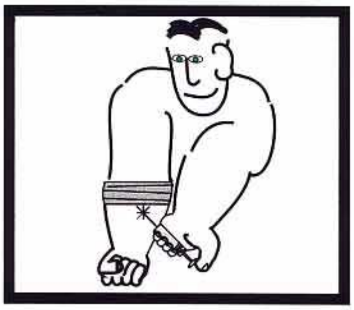
↓

At a later date the viral DNA is transcribed into viral RNA, transported to the ribosomes and viral replication begins.

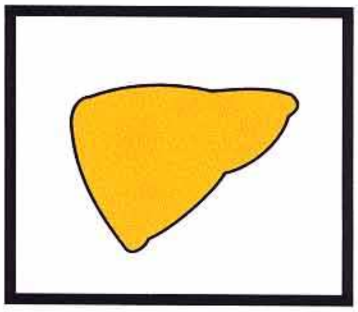
The virus which causes AIDS is an example of a retrovirus.

CAN AN IMMUNE RESPONSE TO A VIRAL INFECTION BE HARMFUL?

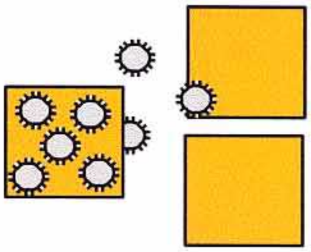
Although looking healthy, this man is actually infected with the hepatitis B virus.



So by using the same needle, the virus can enter his friend's body.

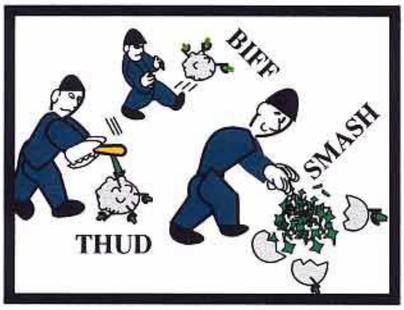


The virus has soon reached and infected his liver.

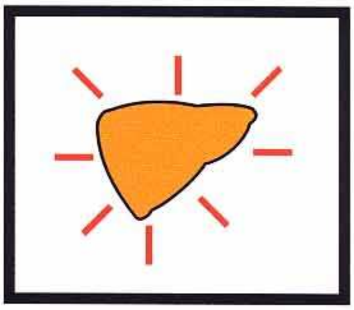


INSIDE THE FRIEND'S LIVER

After replicating inside a liver cell, these emerging hepatitis B viruses enter and infect adjoining liver cells.



Immune cells start to kill the infected liver cells.



The liver becomes acutely inflamed.

Now the patient develops jaundice and is very ill.

THERE ARE NOW 3 POSSIBLE OUTCOMES

1

All the infected cells are destroyed.

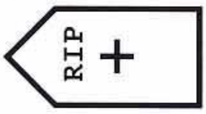
↓

The liver regenerates.

↓

Immunity.

2



All the infected cells are destroyed.

↓

Insufficient liver cells are now left.

↓

Death.

3

Only a few infected cells are eliminated.

↓

The immune assault stops.

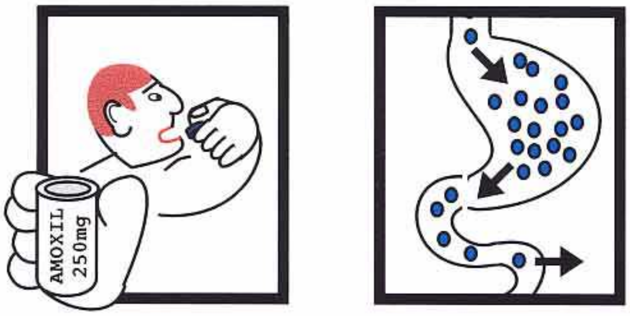
↓

The liver survives but remains infected.

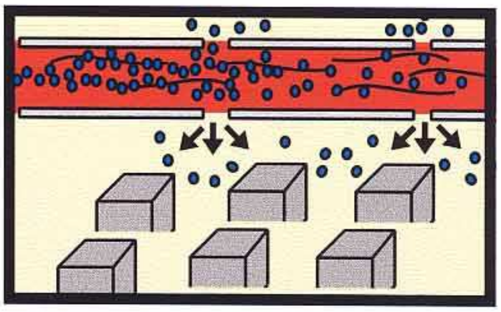
↓

Infected / carrier status for life.

WHY ARE ANTIBIOTICS USELESS FOR VIRAL INFECTIONS?

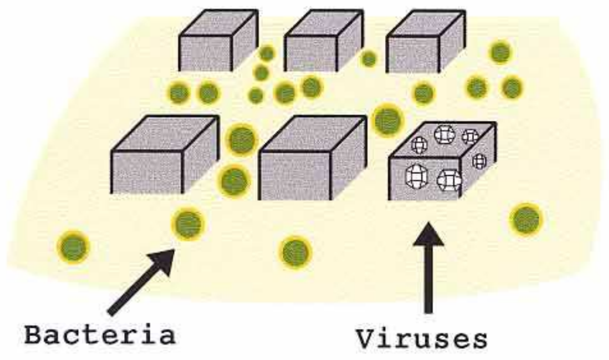


After being swallowed, antibiotics pass out of the gut, into the blood and around the body.

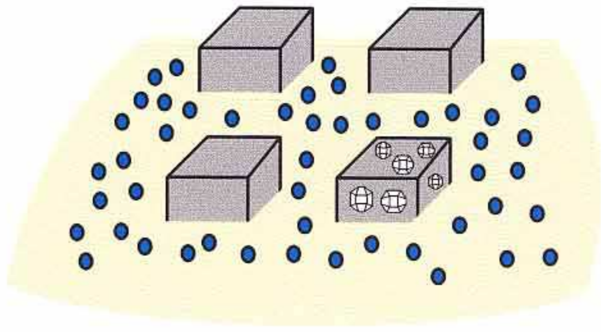


The antibiotics are small enough to pass through gaps in the capillaries and into the tissues.

IN THE TISSUES



While viruses can 'hide' inside cells, most bacteria live out in the 'open'.



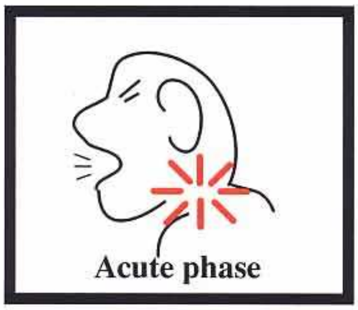
Antibiotics enter the tissues, reach and kill the bacteria but cannot get to the viruses.

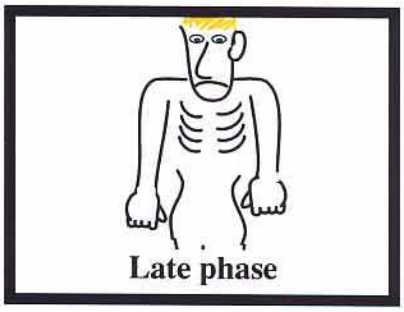
CHAPTER SEVEN

AIDS

FROM HIV INFECTION TO 'FULL BLOWN' AIDS

HIV : Human Immunodeficiency Virus
AIDS : Acquired Immunodeficiency Syndrome





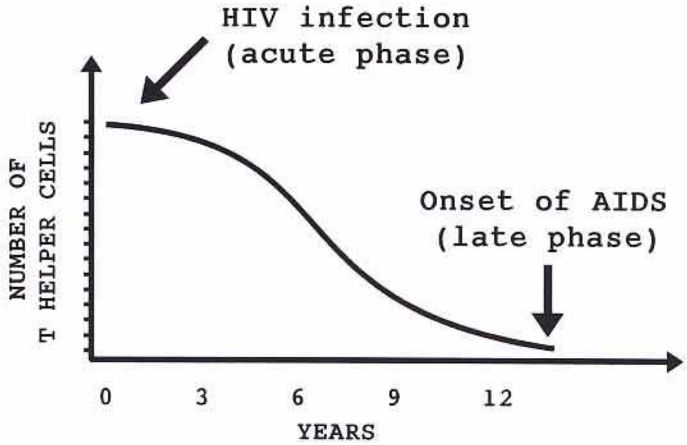
For a few weeks there are strange rashes and flu-like symptoms.

Years can now follow with few, if any, signs or symptoms.

Suddenly, rare cancers and opportunistic infections start to appear.

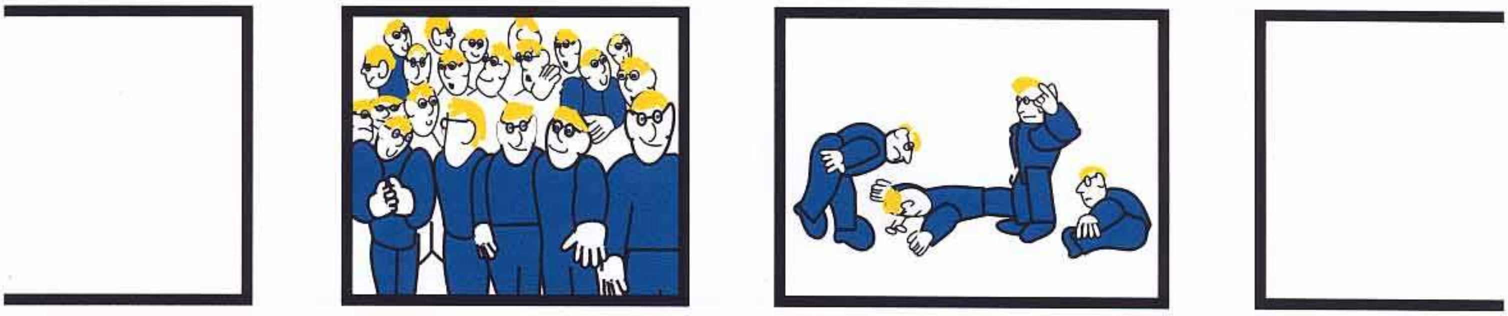
Easy reading

Technical information



Following HIV infection, T helper cell numbers gradually dwindle to nothing.

A PHOTOCALL OF T HELPER CELLS



Just prior to HIV infection.

Many years later and few T helper cells are now left.

With few T helpers left to defend the body, this heralds the onset of 'full blown' AIDS.

THE HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Inside the AIDS virus.

Integrase

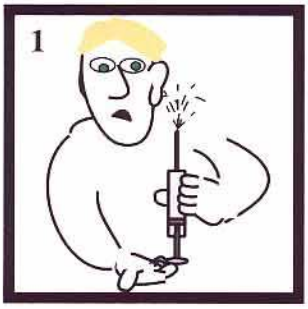
Reverse transcriptase

Viral RNA (see page 130)

Glycoprotein (GP) 120

Glycoprotein (GP) 41

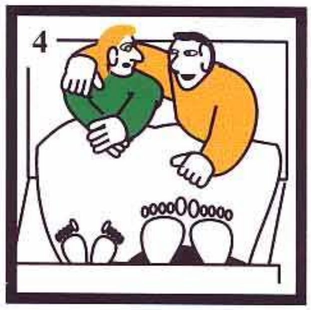
SOME OF THE WAYS PEOPLE BECOME INFECTED BY THIS VIRUS



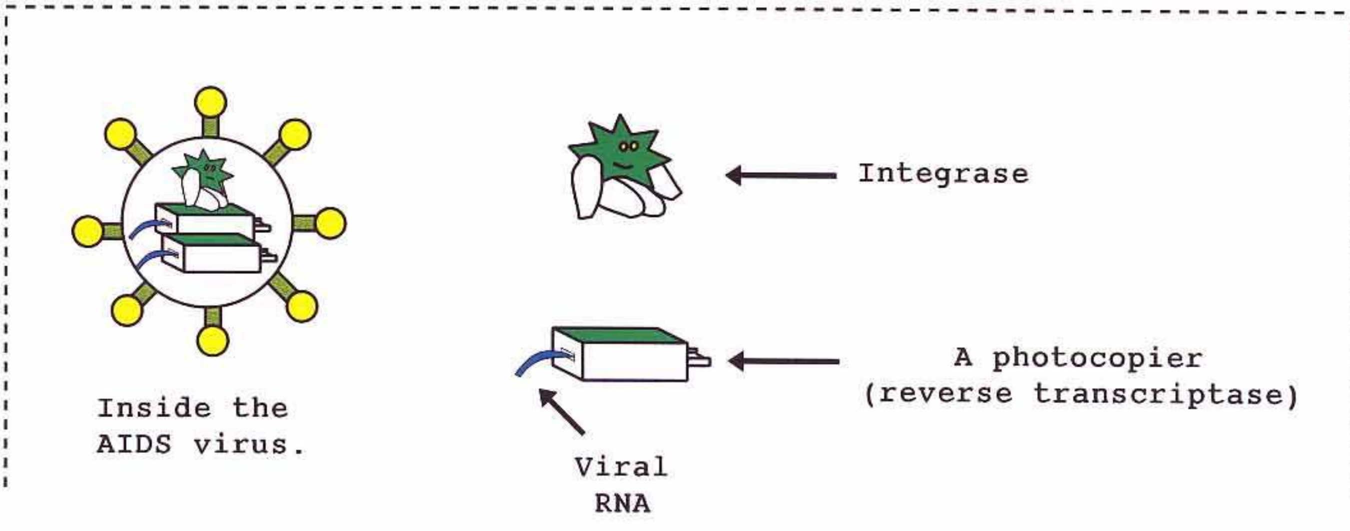
Using a contaminated (infected) needle.

The virus can pass from a mother to her unborn baby.

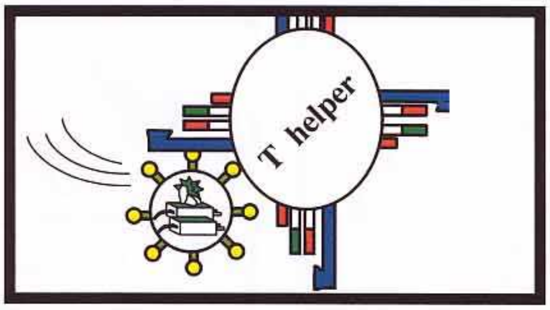
Receiving infected blood products.



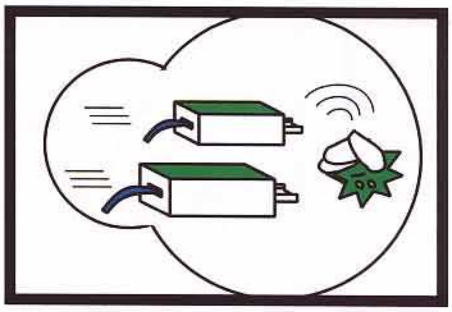
Unprotected sex!!



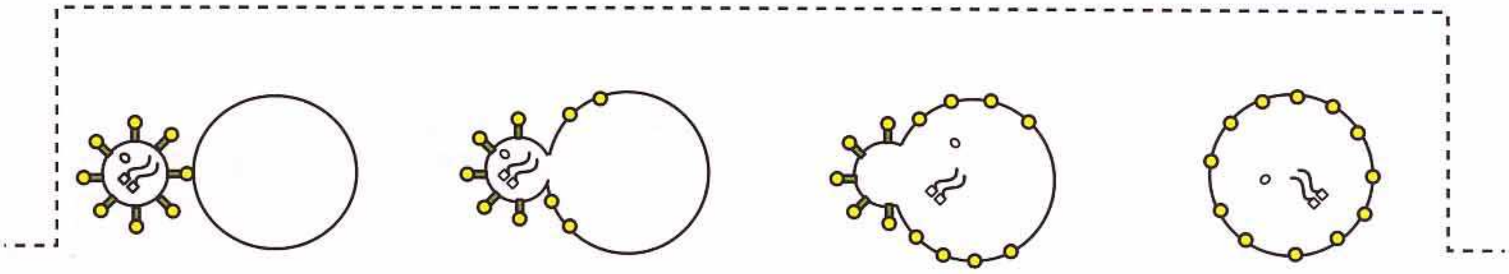
The anti-AIDS drug AZT, works by inactivating reverse transcriptase (the viral photocopiers).



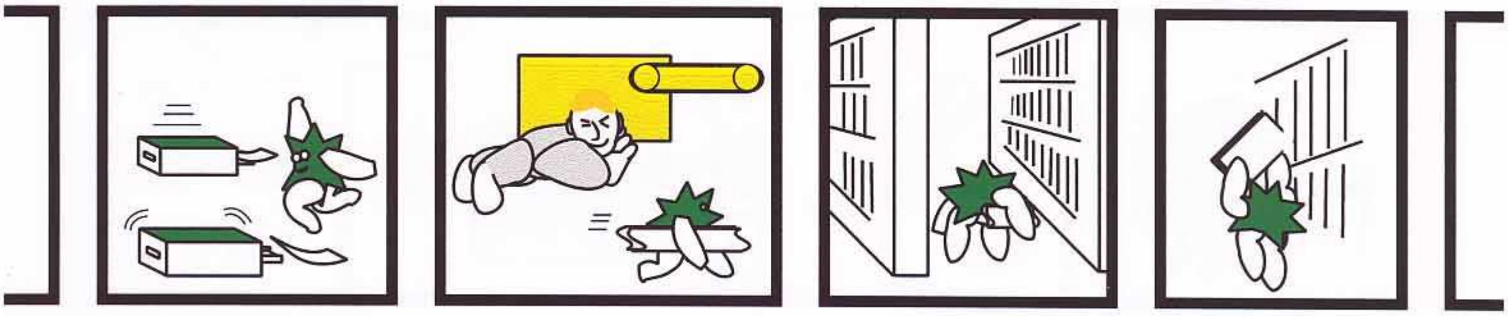
The AIDS virus uses its GP120 protein, to attach onto the T helper's CD4 surface molecule.



Soon its contents have flowed into the T helper cell.



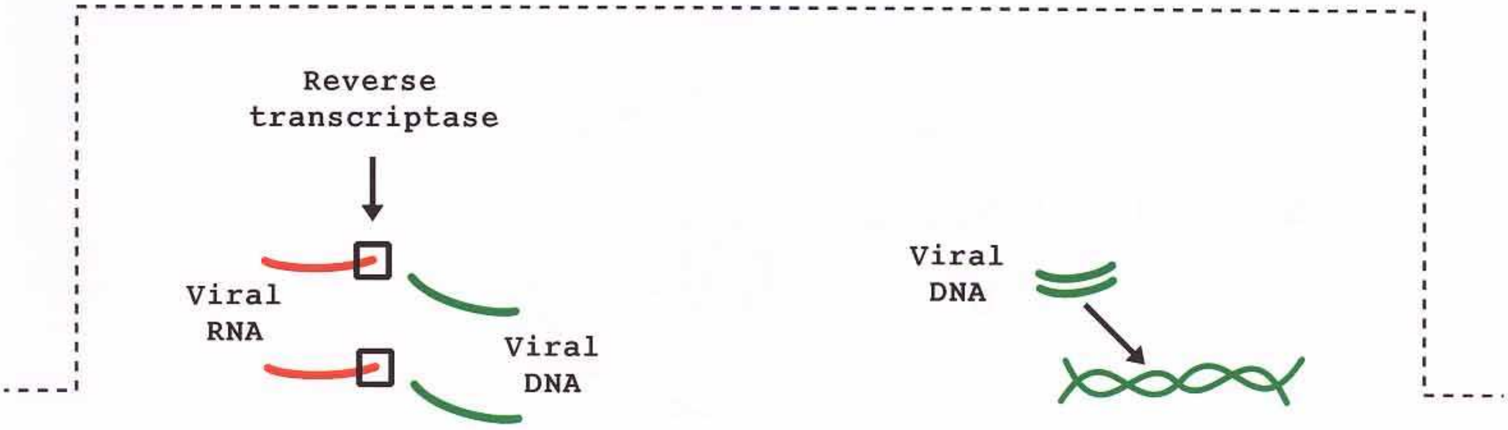
As the 2 membranes fuse together and viral contents flow into the T helper, note how the viral membrane becomes incorporated into the T helper cell's membrane.



The photocopiers start working and release viral DNA.

Integrase now picks up the DNA and takes it into the design centre.

Making his way over to where all the reference books are kept, he slots in his DNA with that belonging to the host.

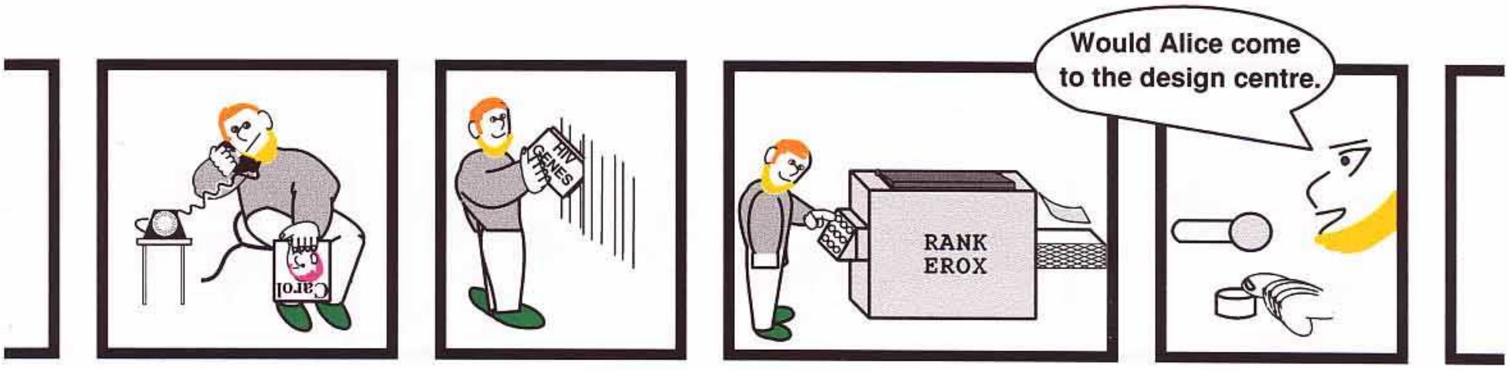


Reverse transcriptase produces viral DNA which is transported into the nucleus.

Integrase then inserts the viral DNA onto one of the host's chromosomes.

WEEKS, MONTHS OR EVEN YEARS LATER

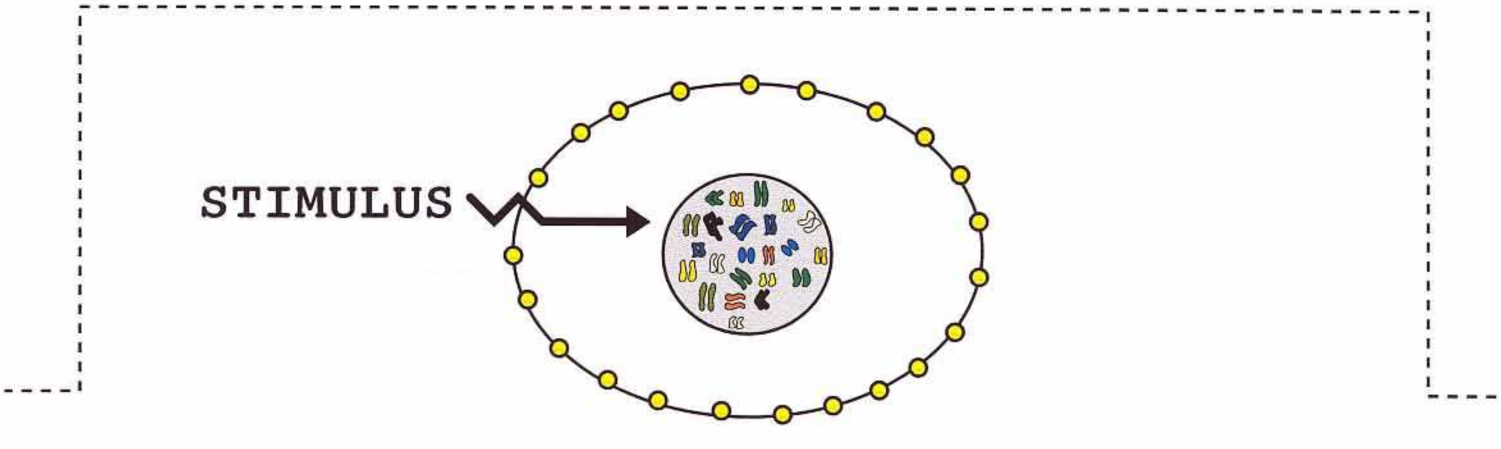
Back inside the infected T helper cell.



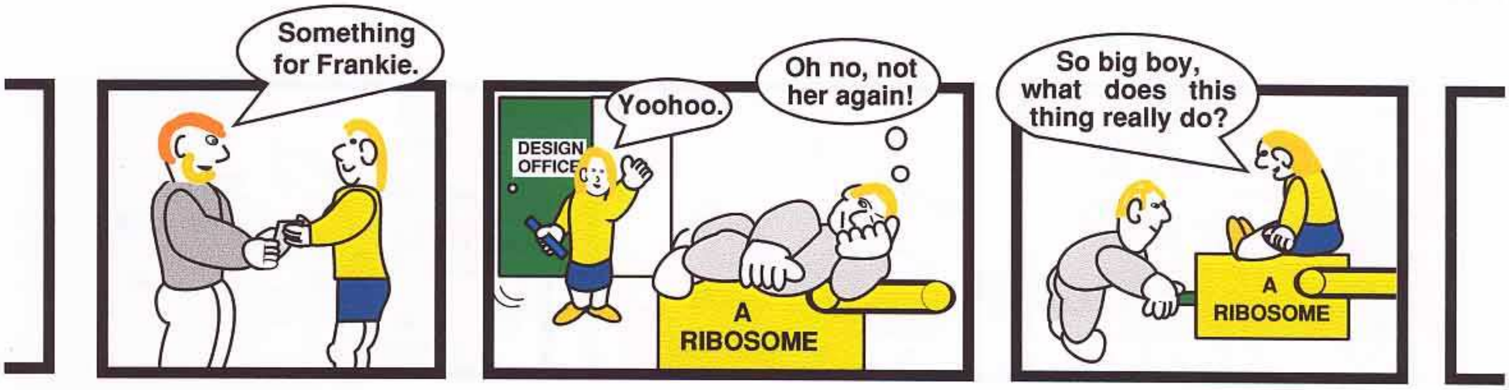
Nick receives a call telling him to start HIV production.

First he finds the HIV manual.

Then it's off to his photo-copier for a messenger RNA copy.



At present it is not known what triggers an infected T helper cell into commencing HIV gene transcription.

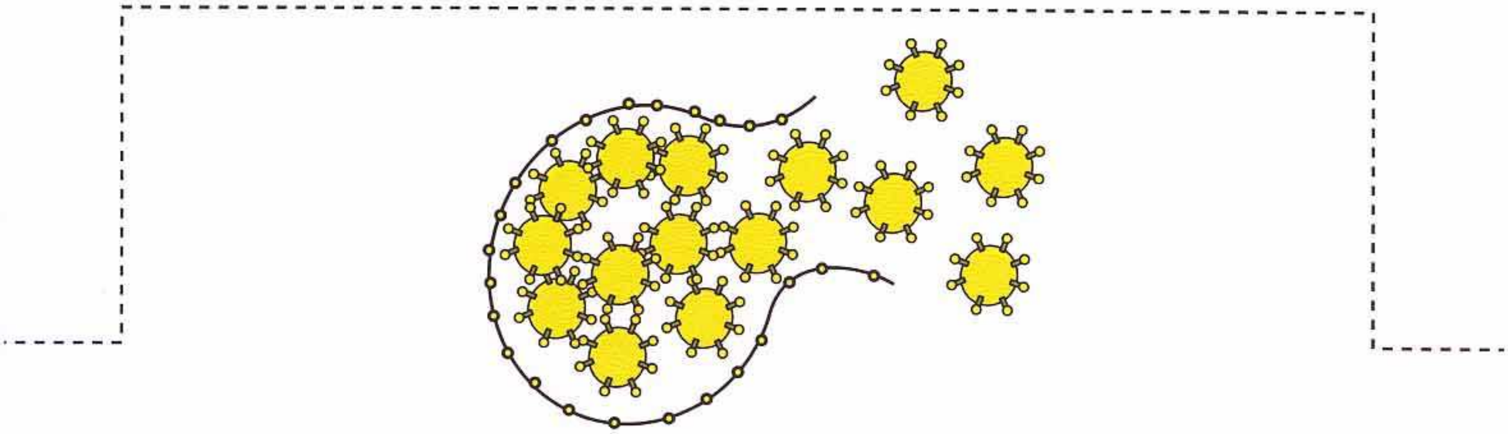


As Nick hands Alice the RNA, he's unaware it will be their death sentence.

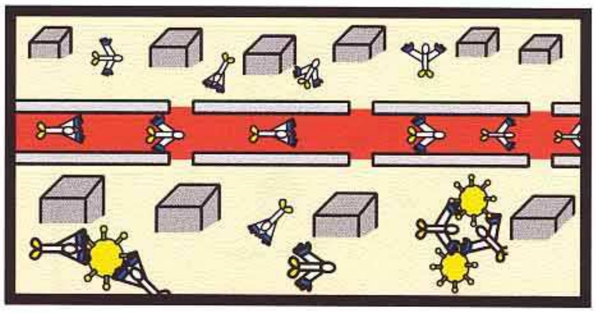
On receiving the RNA, Frankie feeds it into a ribosome.

For ribosomal translation, turn back to page 132.

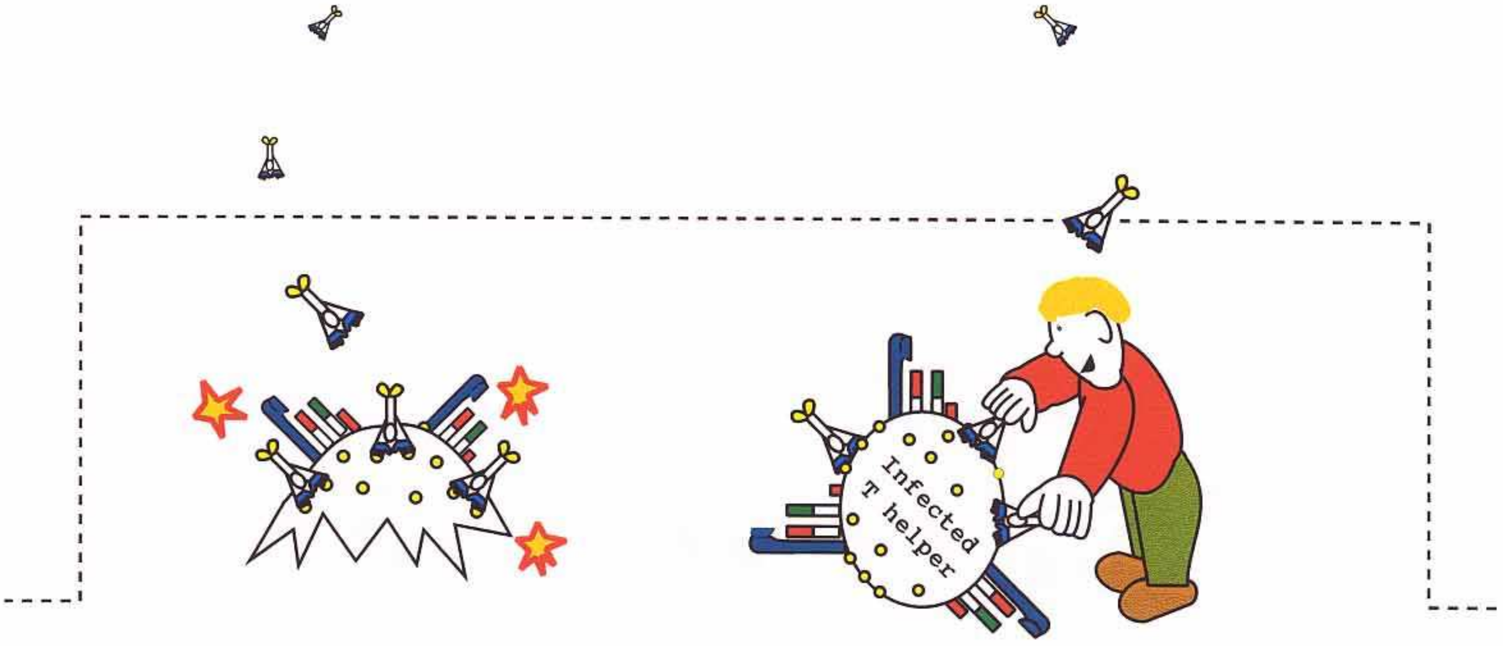
Suddenly from the ribosome, parts of the AIDS virus start appearing.



`Once HIV production starts, it is not long before the infected T helper is filled to bursting point!`



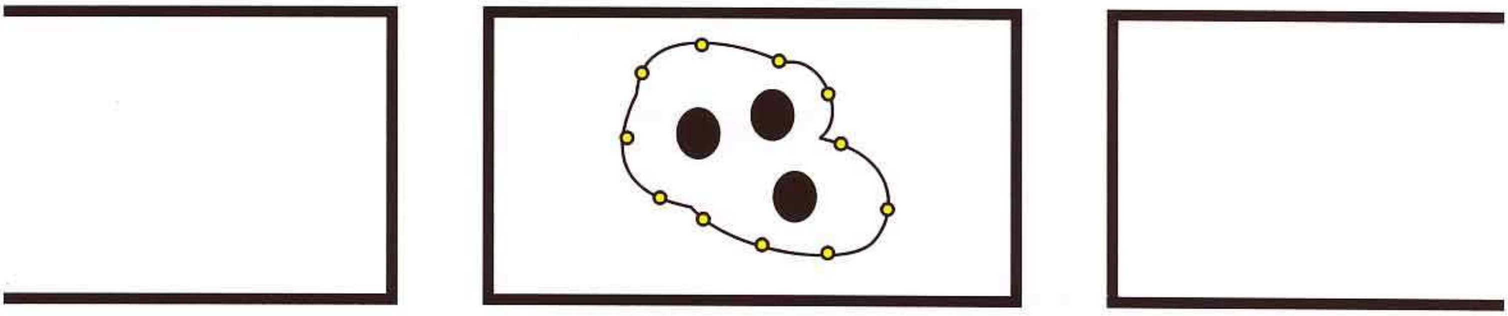
A couple of weeks after becoming infected, anti-HIV antibodies start to appear and quickly mop up any exposed HIV's.



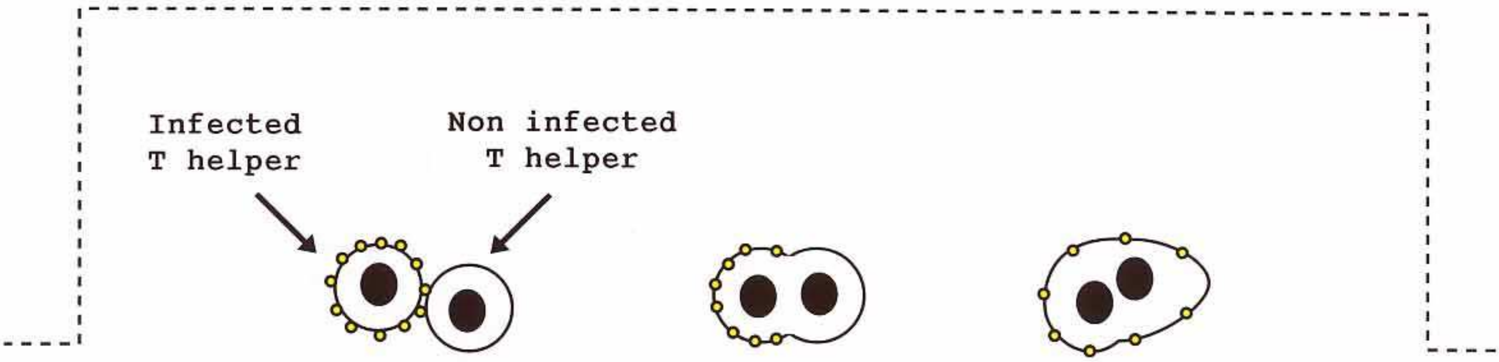
The anti-HIV antibodies may 'grab' viral proteins found on the surface of infected T helper cells. This could then activate complement or encourage macrophages to kill them.

SYNCYTIA

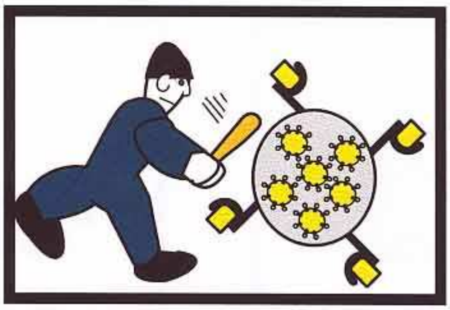
These useless cells, are found in HIV positive (infected) patients.



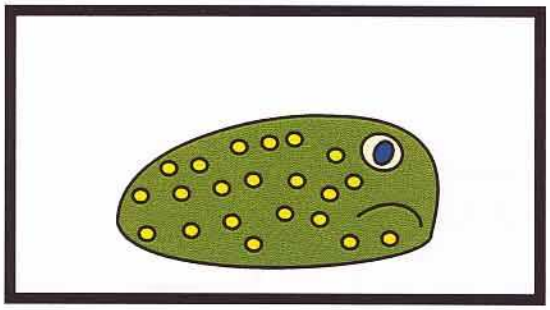
Syncytia are abnormally large multi-nucleated useless T helper cells, which survive for only a short period of time.

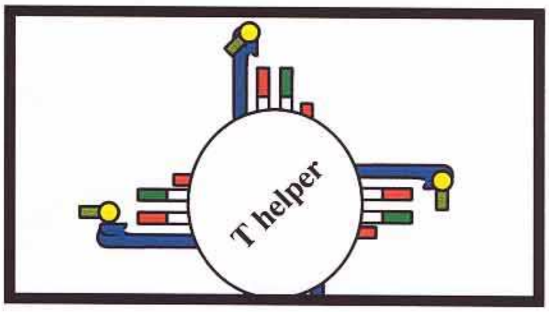


Infected and non infected T helper cells appear to coalesce. This may be due to the HIV proteins found on the surface of infected T helper cells.



Infected T helpers may well be killed off by T cytotoxic cells.





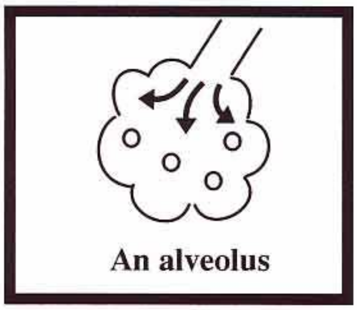
As macrophages can harbour the AIDS virus, this could be a factor in causing declining T helper cell numbers.

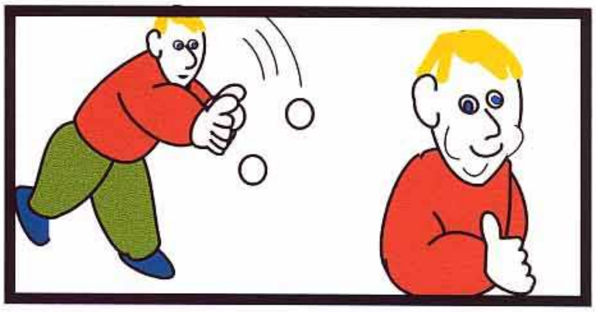
'Free' viral proteins like GP 120, could become attached to uninfected T helper cells and stop them functioning.

Note that both macrophages and T helper cells express the CD4 surface molecule.

PNEUMOCYSTIS CARINII

Although this organism is harmless to most of us, it will kill many AIDS patients.





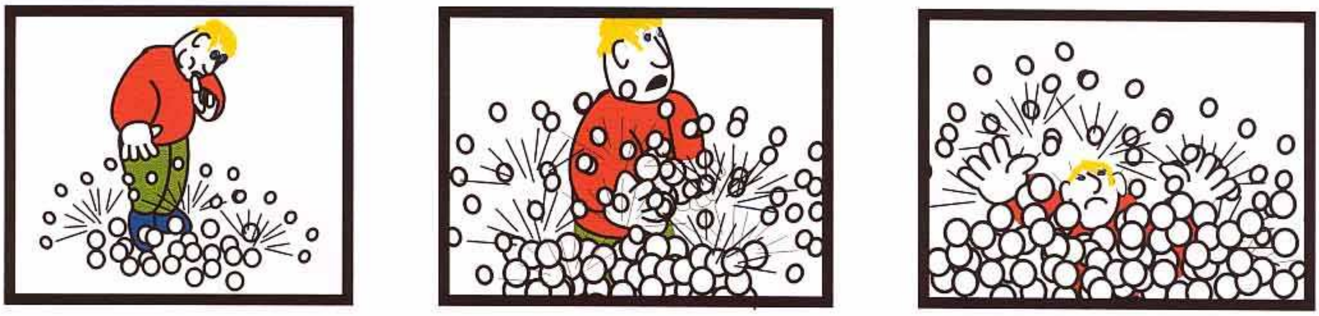
The organism is inhailed into the lungs.

Although these parasites are then 'eaten' by local macrophages, to 'digest' them, they will now need help from the T helper cells.

THE LIFE CYCLE OF PNEUMOCYSTIS CARINII

The parasite enters the lungs as a trophozoite (1). It then enlarges into a cyst with a thick protective coat (2). Sporozoites now develop inside it (3). Soon these burst out to start a new life-cycle as trophozoites (4).

SOON THE LUNGS START TO CLOG UP

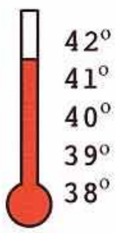


AIDS patients have few if any T helper cells to now assist the alveolar macrophages. So the trophozoites and cysts are not eradicated and these begin to 'fill up' the victims lungs. Soon a life-threatening pneumonia develops, which unfortunately, is frequntly fatal.

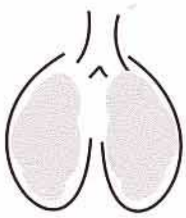
ASSOCIATED SIGNS AND SYMPTOMS

Rapid breathing.

TEMP (C)



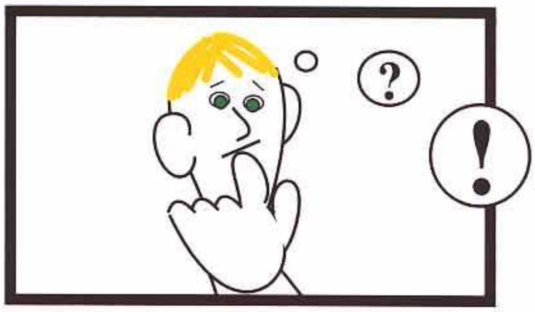
A raised temperature.



X-rays show both lungs are affected.

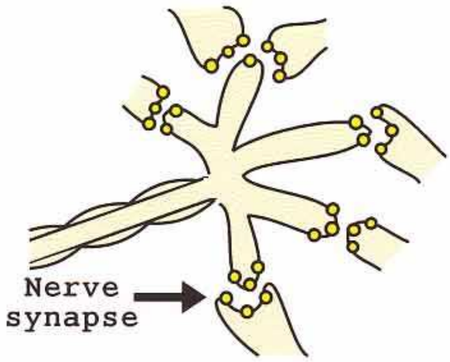
A lung biopsy.

NEUROLOGICAL COMPLICATIONS

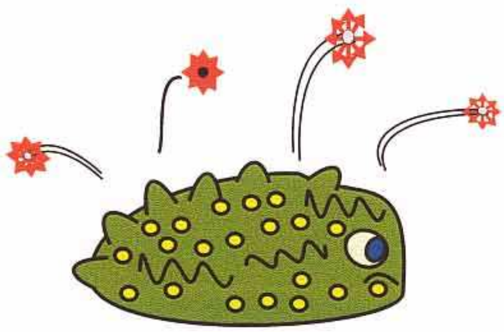


Many people suffering from AIDS develop memory loss and dementia.

POSSIBLE CAUSES FOR THE MEMORY LOSS AND DEMENTIA



Viral particles like GP 120, might become attached to nerve synapses in the brain, disrupting normal neurological function.

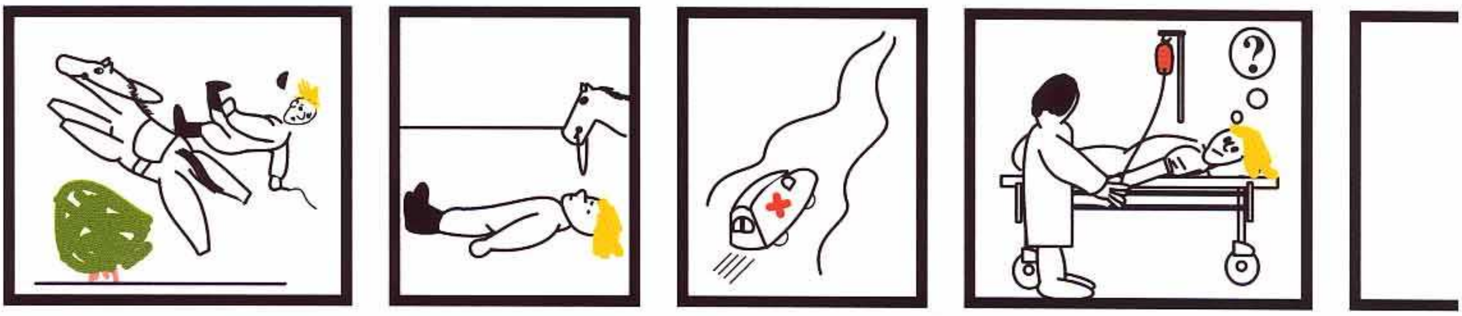


Infected brain macrophages might release excessive amounts of inflammation, which could harm the brain.

CHAPTER EIGHT

THE RED BLOOD CELL

BLOOD GROUPS

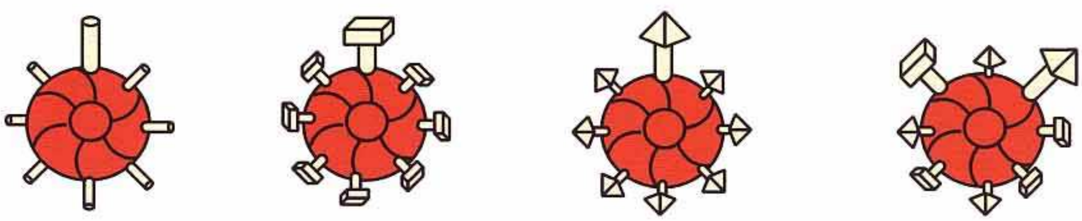


Following a riding accident, Holly is rushed to hospital for a blood transfusion.

Easy reading

Technical information

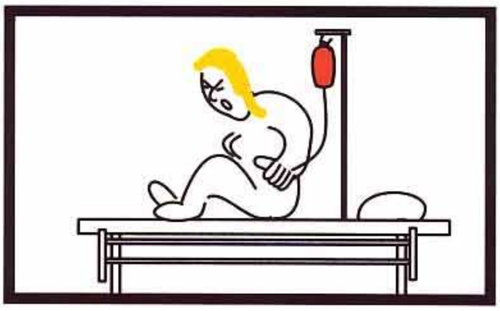
THE ABO BLOOD GROUPS



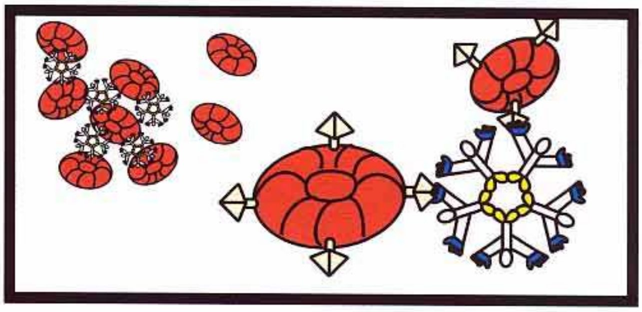
Group O Group A Group B Group AB

The only difference between these blood groups are 2 surface markers, found at the end of the common O core.

HOLLY IS GIVEN THE WRONG BLOOD GROUP

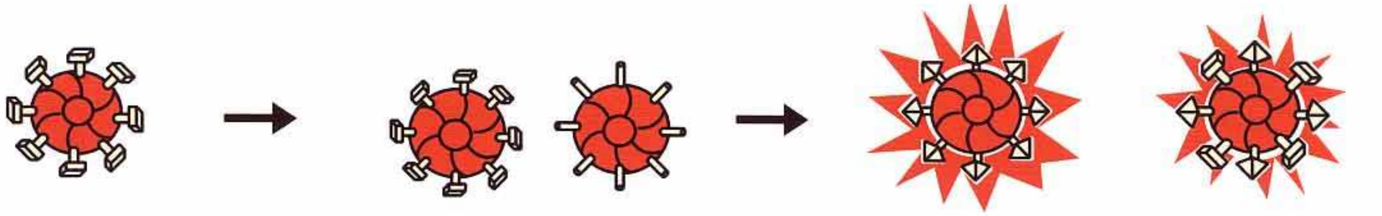


But only minutes after starting the blood transfusion, Holly begins to experience severe back pain.

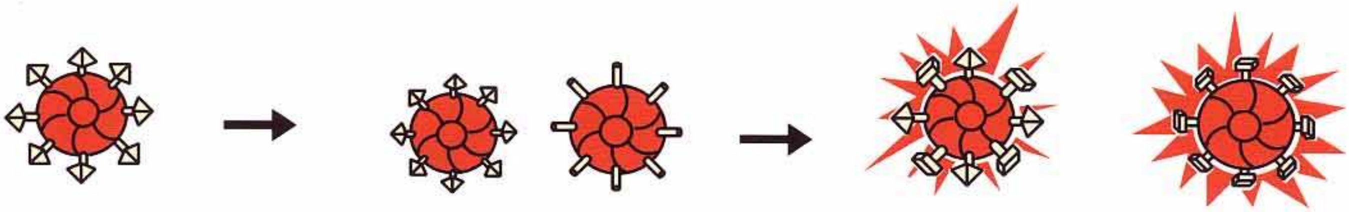


IgM antibodies in her blood have 'grabbed' the transfused red blood cells and the resulting complexes start to block her kidneys.

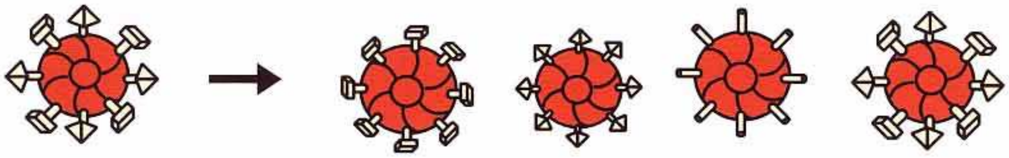
For an unknown reason, soon after we are born, our immune system will start to produce IgM antibodies with 'hands' which fit any ABO blood group marker, not found on our own red blood cells.



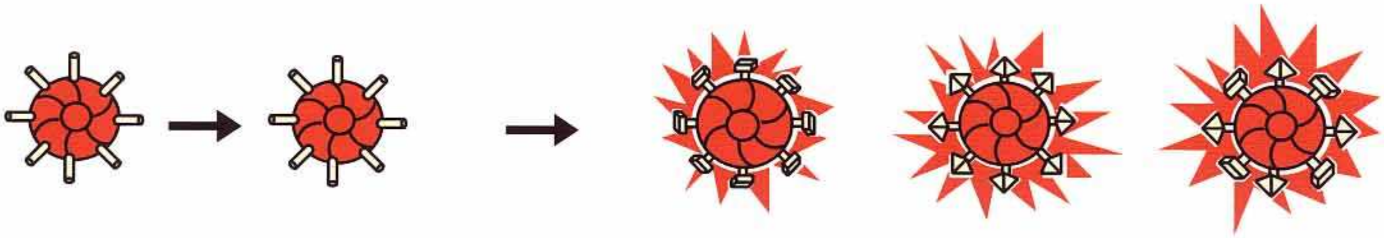
Group A patients can receive blood groups A and O. **But they will reject groups B and AB.**



Group B patients can receive blood groups B and O. **But they will reject groups A and AB.**



Group AB patients can receive any ABO blood group (ie A, B, AB and O). Hence, these patients are sometimes referred to as the 'universal recipient'.

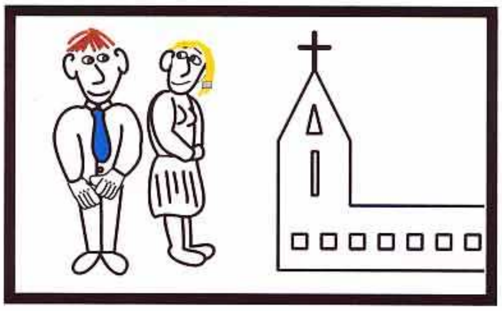


Group O patients can only receive group O blood. **They will reject the other ABO blood groups.**

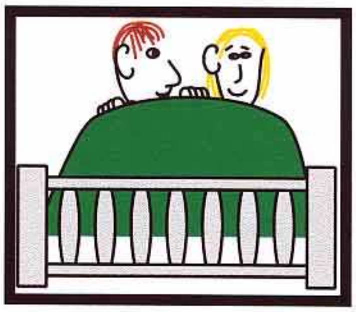
Because group O blood does not have either the A or the B surface markers, it can be given to patients with the other ABO blood groups. Hence group O patients are sometimes referred to as 'universal donors'.

THE RHESUS FACTOR

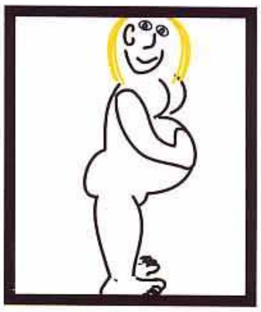
About 60% of the population have this molecule on their red blood cells.



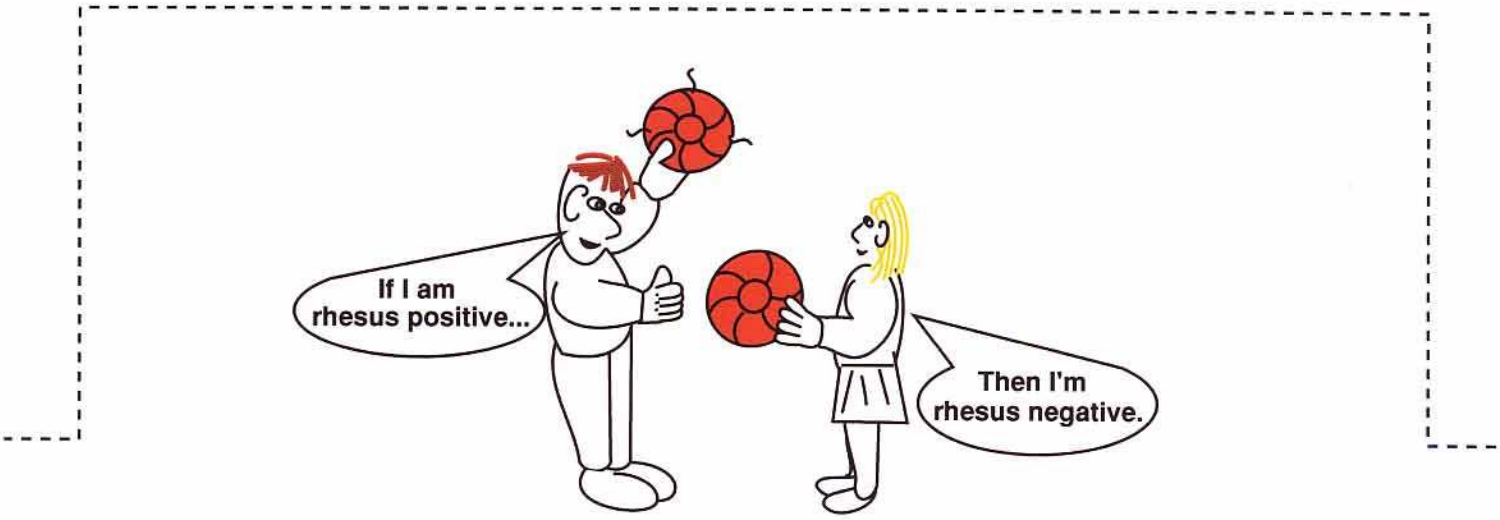
Dan and Rosie decide to tie the knot.



He pops the question.

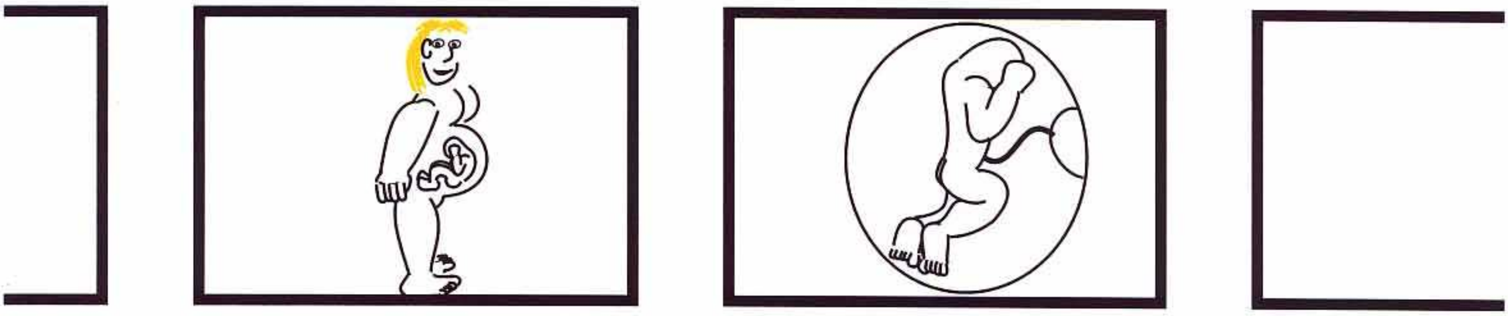


4 months later!



Dan has the rhesus factor on his red blood cells (RBC's). But unfortunately, Rosie does not have it on her's.

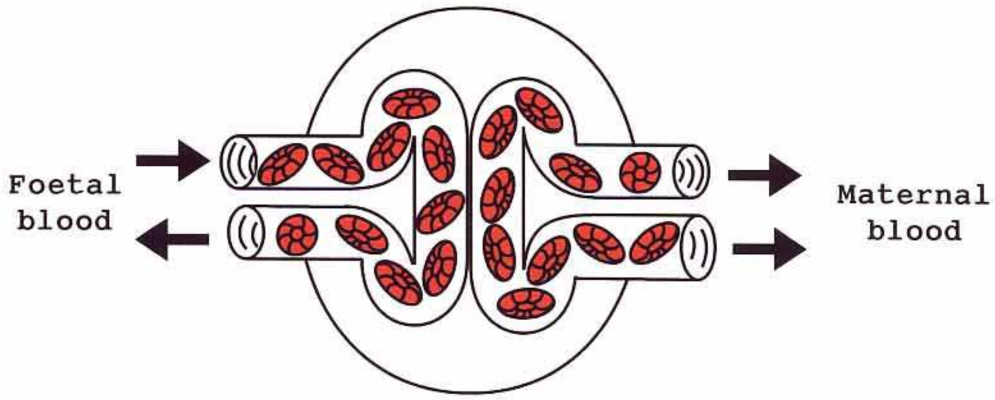
LIKE DAD, THE FOETUS IS RHESUS POSITIVE



As you can see, Rosie's baby is now growing rapidly inside her.

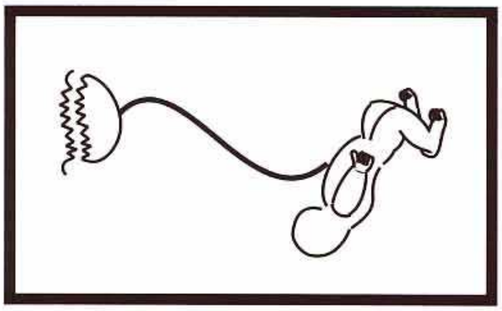
All the unborn baby's nutrients must come via the placenta.

THE PLACENTA

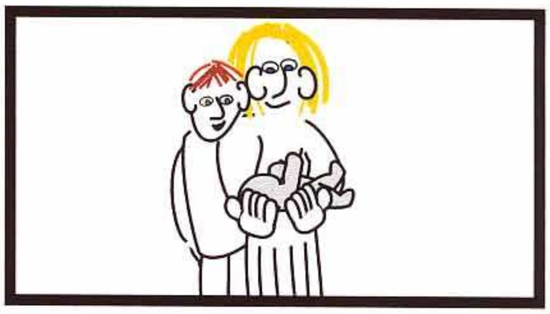


In the placenta, the baby's and maternal RBC's remain separated.

AT THE BIRTH

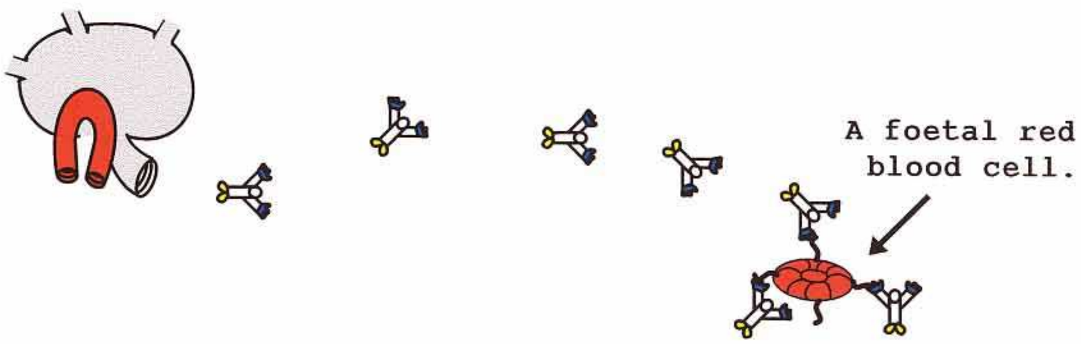


After the baby is born, the placenta detaches and foetal blood sometimes enters the mother's circulation.



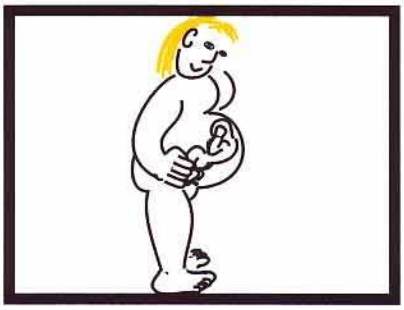
Dan is chuffed about their first baby, but is unaware that some of its blood has mixed with Rosie's blood.

2 WEEKS LATER, INSIDE ROSIE

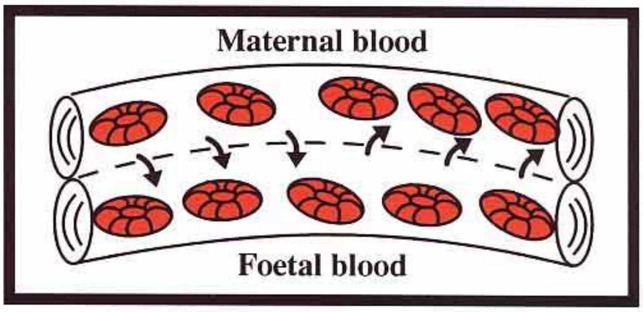


Because RBC's coated with the rhesus factor are foreign to Rosie's immune system, IgG are released to eliminate them.

SEVERAL YEARS LATER

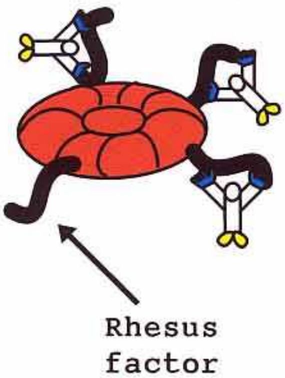


Rosie has baby number 2, which is also rhesus positive.



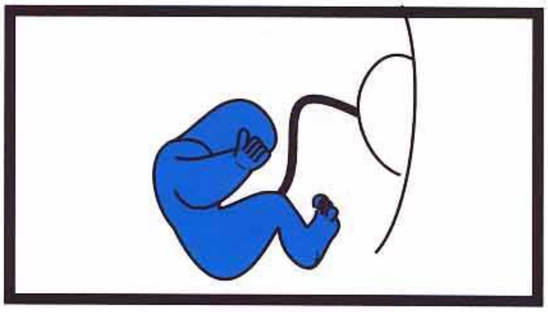
In the placenta, small things like the mother's anti-rhesus IgG (made after the birth of her first baby), pass from the mother to her foetus.

INSIDE THE FOETUS



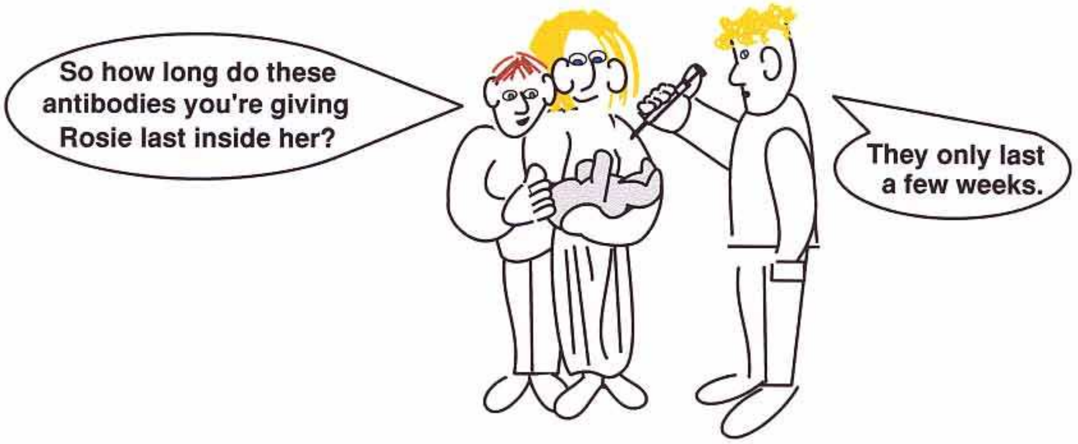
The mother's anti - rhesus IgG, 'grab' the rhesus factor on the foetal RBC's, but are not close enough to activate complement.

However, the baby's own macro-phages now 'think' that the red blood cell's are foreign and start to 'eat' them.



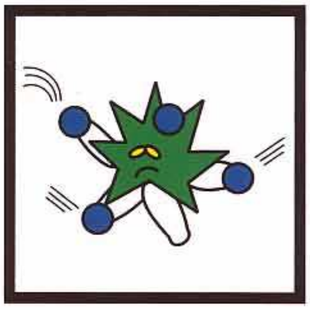
As the foetal macrophages remove the coated red blood cells, so the foetus becomes anaemic and could die.

PREVENTION

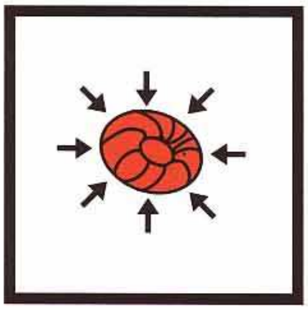


So whenever a rhesus negative mother gives birth to a rhesus positive baby, she will be given anti - rhesus antibodies. These will 'grab' any foetal RBC's now inside her, before her immune system is triggered into making any anti-rhesus IgG.

A FEW OTHER FACTS ABOUT RBC's



This microbe has been coated in complement C3b.

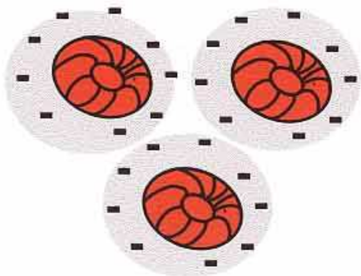


RBC's have surface receptors which will fit C3b (see page 267).

Once attached to a RBC, the microbe is soon being carried to the spleen.

In here, it is plucked off and 'eaten' by the resident macrophages.

The red blood cell or erythrocyte (as it is sometimes called), carries oxygen around the body.



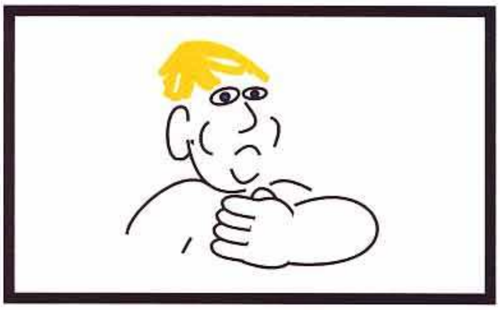
Each RBC carries a small negative charge, called a "zeta potential", which repels neighbouring RBC's.

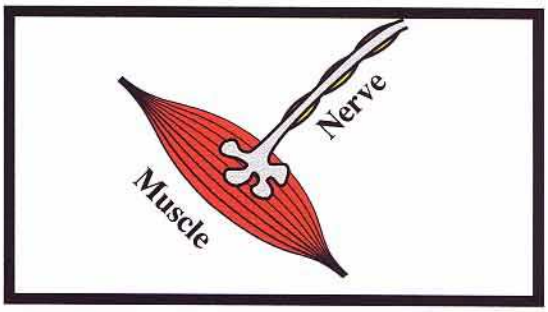
CHAPTER NINE

AUTOIMMUNITY

MYASTHENIA GRAVIS

A hard act to swallow!



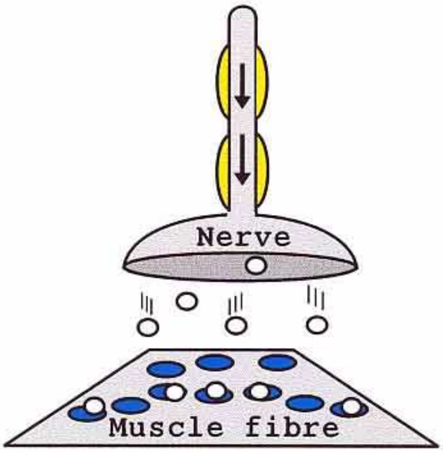


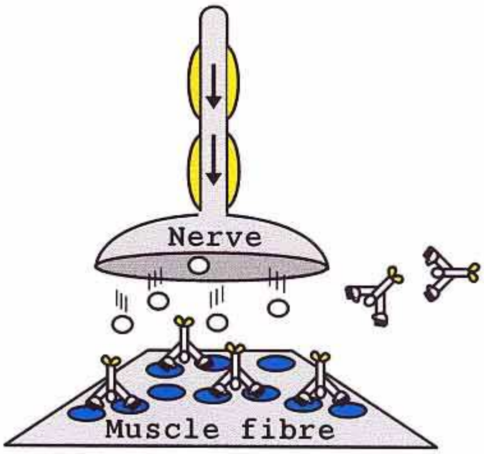
This man is having difficulty with breathing, chewing and swallowing.

These problems are caused by nerve impulses not reaching certain muscles.

Easy reading

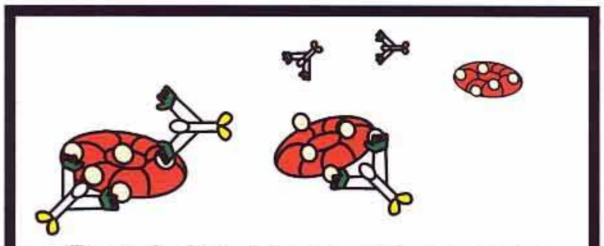
Technical information



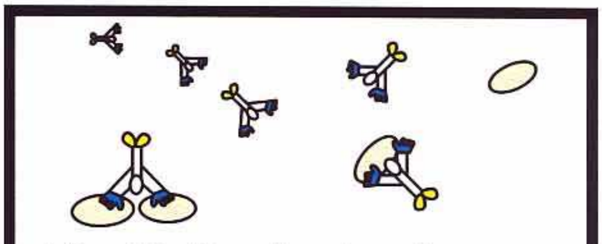


Normally, nerve impulses reaching the end of a nerve, cause the release of acetylcholine onto the muscle fibre.

With this disorder, antibodies are made which have 'hands' that fit the acetylcholine receptors and so block the nerve impulse.



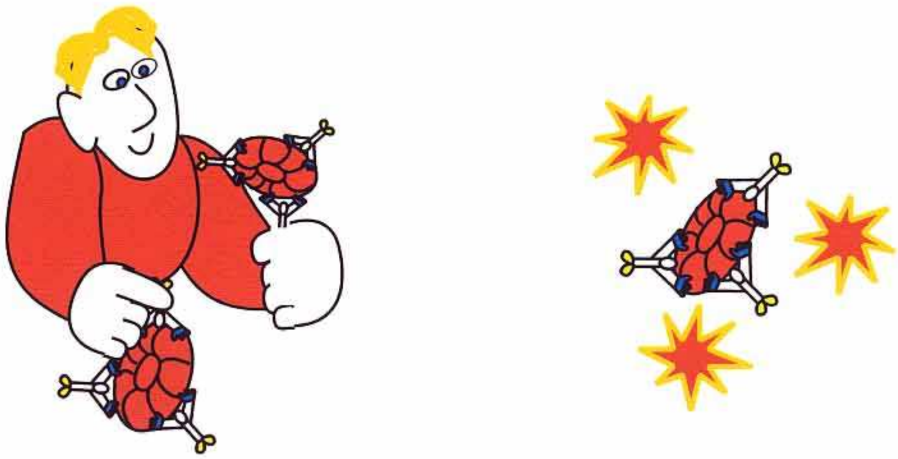
Drug-induced haemolytic anaemia



Idiopathic thrombocytopenic purpura

Occasionally, when drugs like penicillin become bound to cells such as RBC's, this can trigger an immune response.

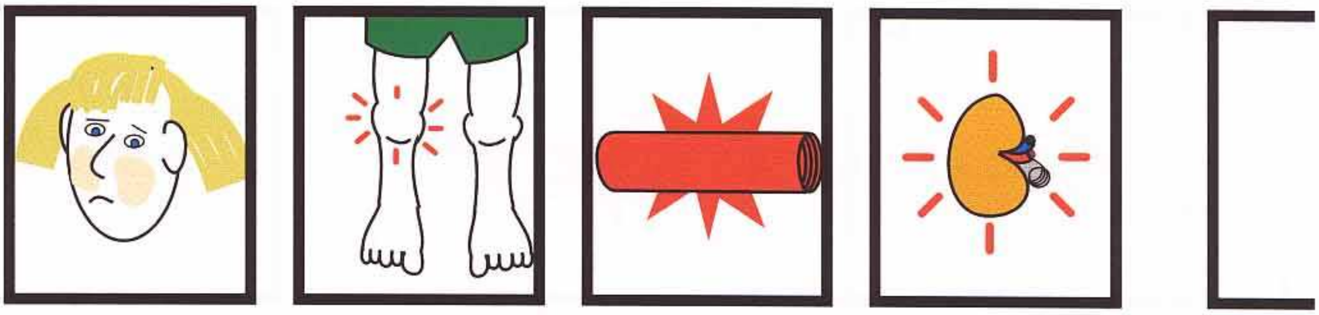
But on other occasions, for no apparent reason, the immune system eliminates useful cells such as platelets.



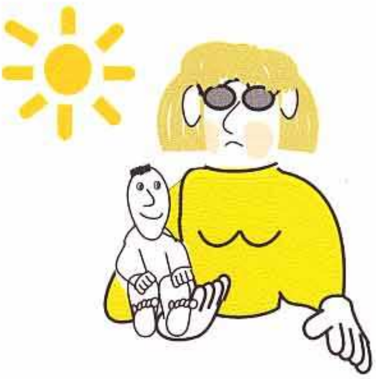
Once something becomes coated in antibodies, it will be 'eaten' by macrophages in the spleen or the liver, or 'blown apart' by complement.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

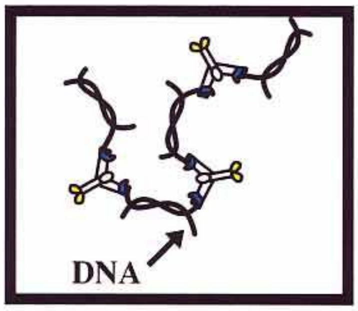
Making a rash decision.



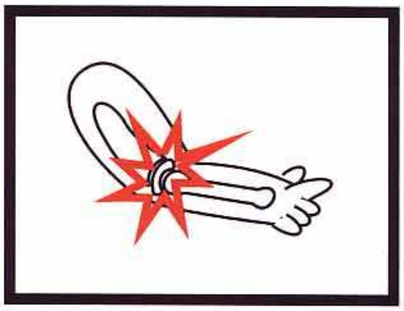
As its name suggests, this condition affects the whole body, with symptoms such as:- facial rashes, arthritis, arterial inflammation and kidney damage.



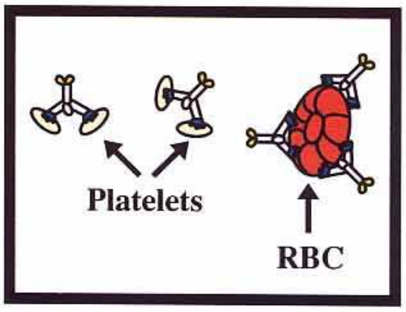
Tending to 'run' in families, this autoimmune disorder is made worse by ultraviolet light and affects 10 times more women than men.



Antibodies with 'hands' fitting the patients own DNA, start to appear.

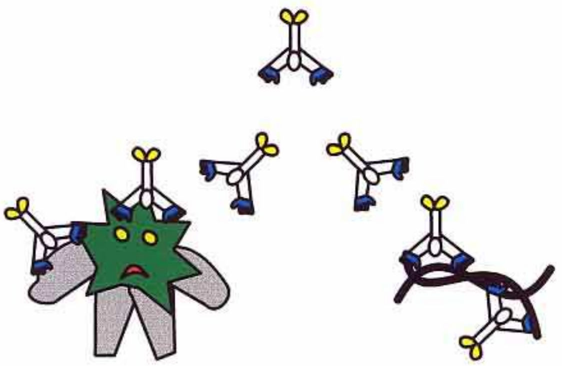


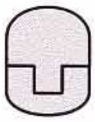
These complexes then become trapped in the joints and kidneys, activating complement.



RBC's and platelets can also be targetted, causing bleeding disorders and anaemia.

Worn out cells are constantly being broken down. This releases DNA into the circulation. Although this is not a problem for most of us, SLE patients make anti-DNA antibodies.





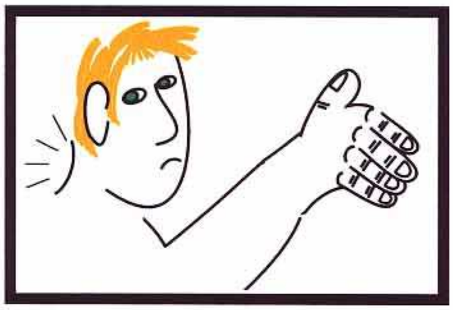
Complement C4
(see page 266)

SLE sufferers make antibodies against certain microbes such as the klebsiella bacteria, which also fit their own DNA.

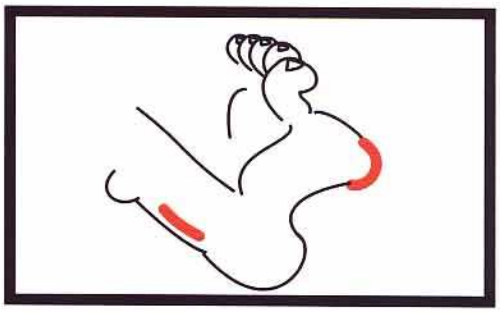
As they also often lack complement C4, it may be harder for macrophages to eliminate immune complexes, which then get trapped in the wrong places!

RHEUMATOID ARTHRITIS (RA)

A bone of contention.

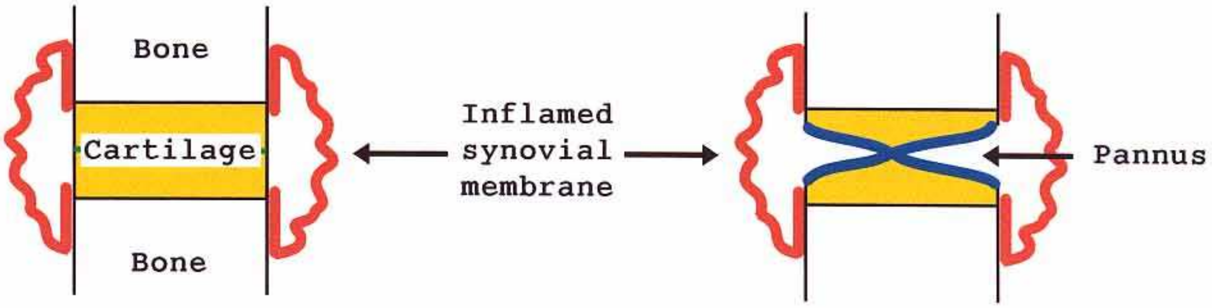


This chronic connective tissue disorder frequently produces deformed, painful joints.



Other features common to RA, include:- subcutaneous nodules and inflamed tendons and bursas.

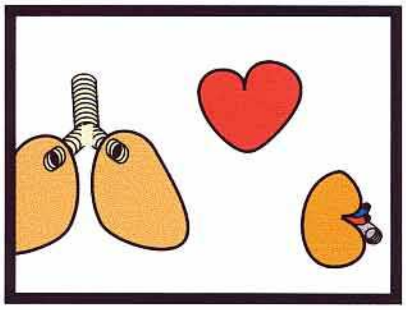
AN AFFECTED JOINT IN A RHEUMATOID PATIENT



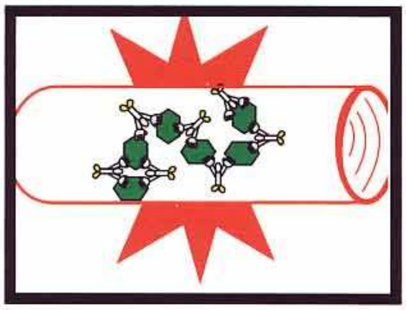
First there is acute inflammation of the synovial membrane.

Then enzymes slowly digest the cartilage and pannus spreads over the articulating surface.

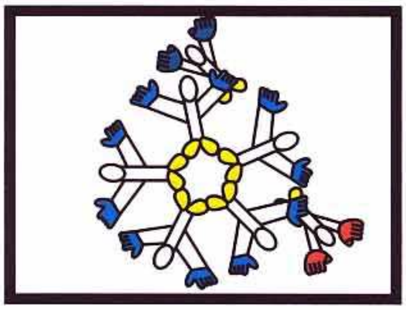
OTHER COMMON FEATURES ASSOCIATED WITH RA



Chronic joint inflamation associated with this auto-immune disorder, sometimes causes a prolonged acute phase response. This can lead to damaging amyloid deposits being laid down in the lungs, heart and kidneys.



Immune complexes can become trapped in the patient's blood vessels, activating complement and triggering an inflammatory response (vasculitis).

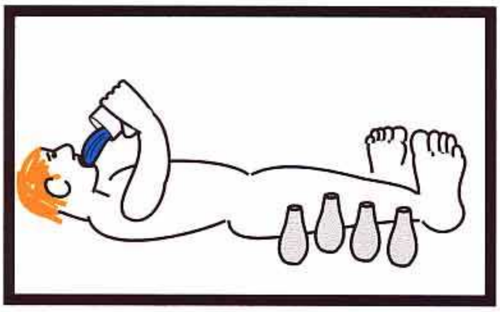


Rheumatoid patients frequently produce rhematoid factors, which are IgG or IgM antibodies with 'hands' that fit the 'bodies' of other antibodies.

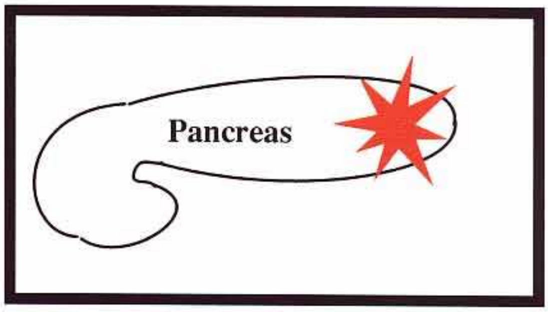
Although the cause or causes of rheumatoid arthritis are not known, it often recurrs in families. It affects many more women than men and usually first appears between the ages of 30 and 40.

INSULIN - DEPENDANT DIABETES MELLITUS

A sweet little mystery.

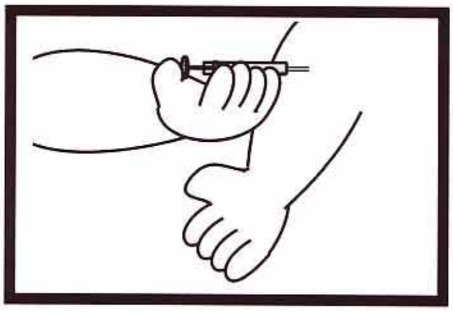


James feels lethargic, is constantly thirsty and is passing 'gallons' of dilute urine.

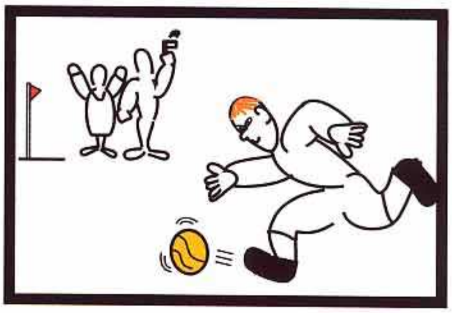


For an unknown reason, his immune system has destroyed the insulin prod-ucing beta cells in his pancreas.

Insulin released from the pancreas, enables cells in the the body to absorb glucose.

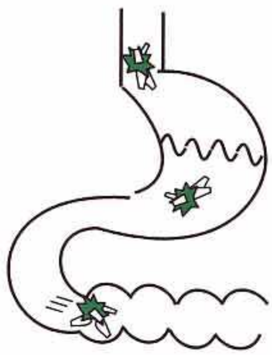


So from now on he must have daily insulin injections.



Soon James is back to normal and feeling full of energy!

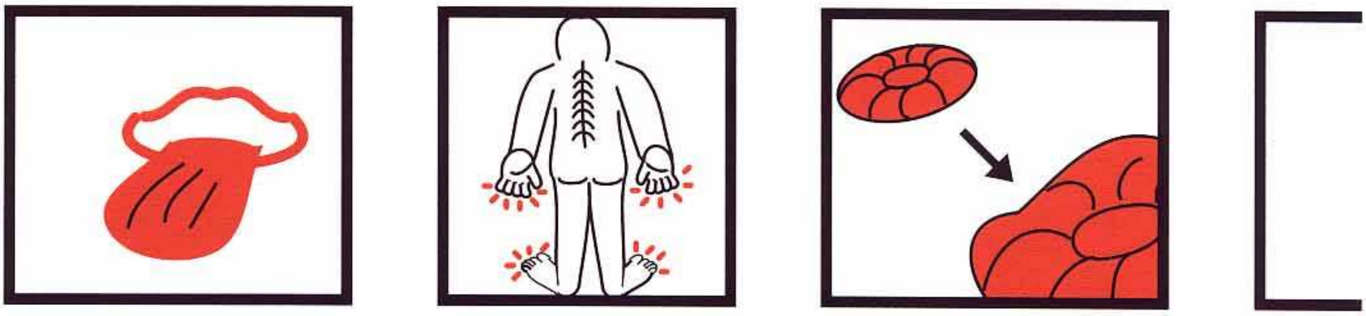
Frequntly starting before the age of 30, insulin-dependant diabetes seems to 'run' in families.



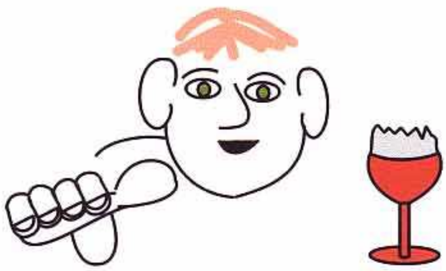
The onset of this disorder, frequently follows a viral infection, by organisms such as the coxsackie enterovirus.

PERNICIOUS ANAEMIA

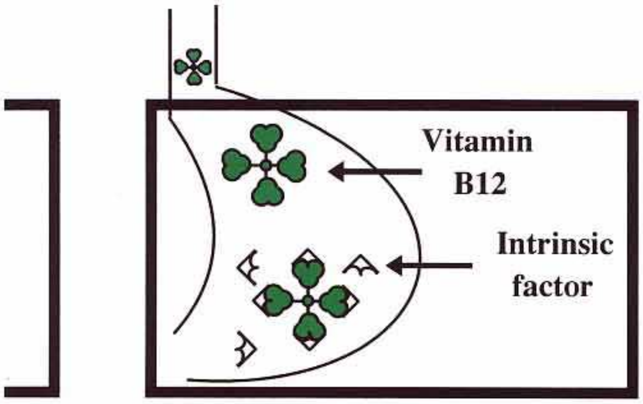
If you cannot stomach this,
it will get on your nerves.

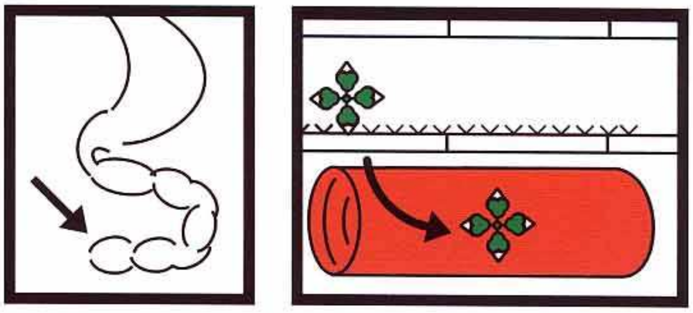


Signs and symptoms commonly associated with this autoimmune disorder include:- a smooth tongue, 'pins and needles' in the feet and hands and enlarged RBC's.



It occurs when the body is unable to absorb vitamin B12, which is found in foods such as eggs.

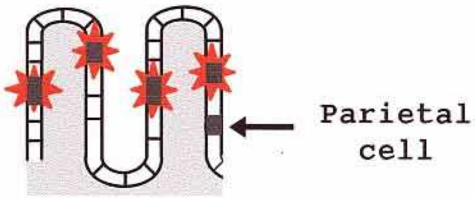




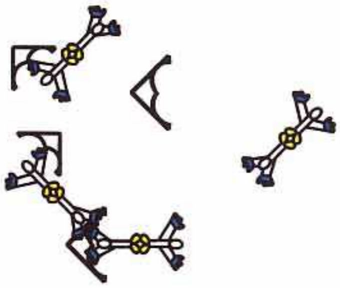
Normally, when vitamin B12 enters the stomach, it becomes coated in intrinsic factor.

These complexes then passes on to the terminal ileum, where receptors lining this part of the gut transport them into the bloodstream.

Pernicious anaemia develops when intrinsic factor ceases to appear.



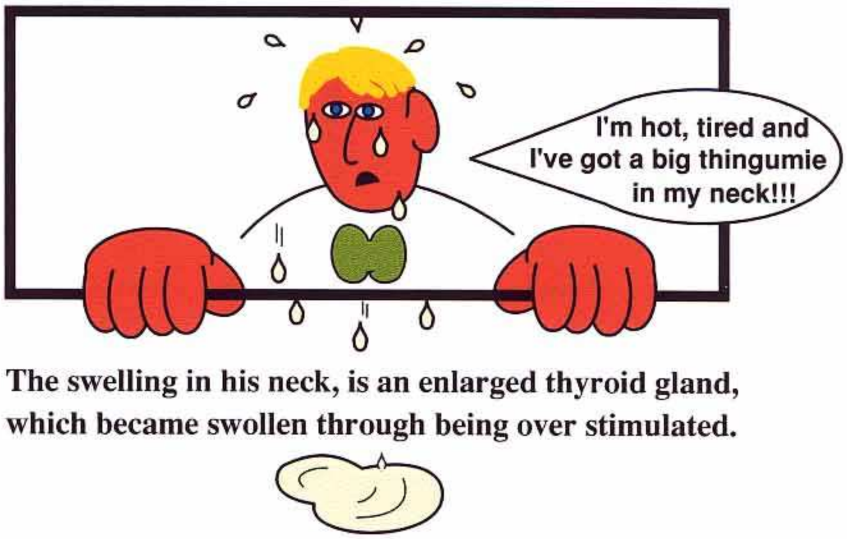
In the stomach, immune cells destroy the parietal cells which make intrinsic factor.



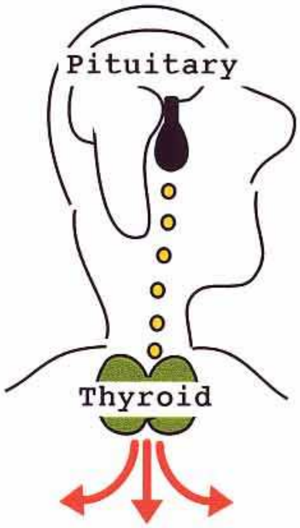
IgA with 'hands' that fit intrinsic factor, are also produced.

GRAVES' DISEASE

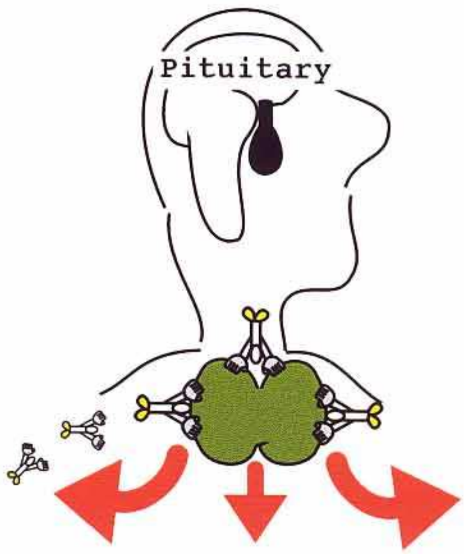
Geting all hot under the collar!



The swelling in his neck, is an enlarged thyroid gland, which became swollen through being over stimulated.

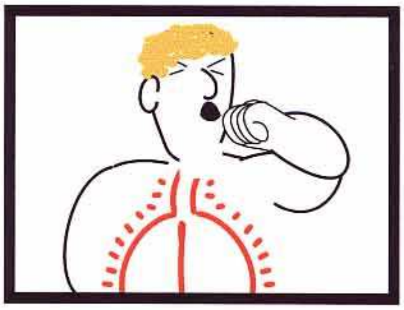


The amount of thyroxine released by the thyroid, is normally controlled by the pituitary gland.



With Graves' disease, auto antibodies attach onto the thyroid, causing its over-stimulation and excessive release of thyroxine.

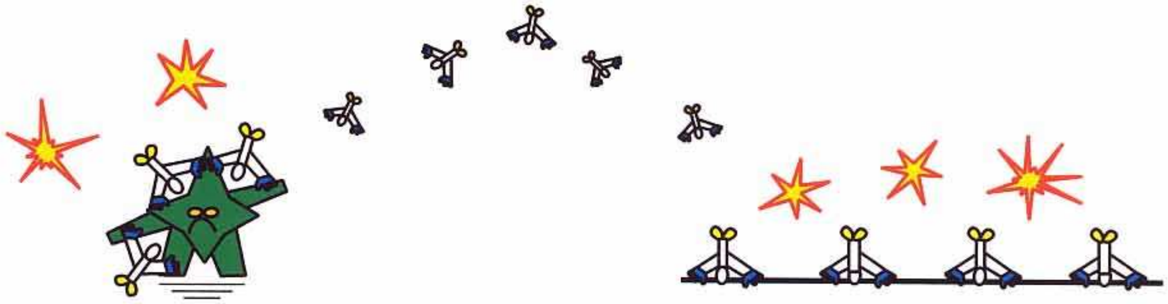
GOODPASTURE'S SYNDROME



Charlie develops a routine chest infection caused by the influenza A2 virus.

But 2 weeks later he starts to cough up blood and have problems with his kidneys.

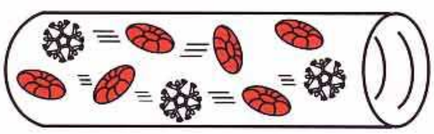
WHAT WENT WRONG WITH THIS IMMUNE RESPONSE?



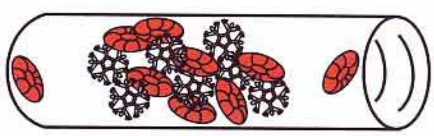
After a couple of weeks, antibodies with 'hands' fitting the virus appear.

Unfortunately their 'hands' also fit type 4 collagen, in the kidneys and lungs.

If Peter goes out in cold weather without enough clothing, he experiences extreme pain in his limbs, which only resolves when he is back in the warm.



Warm conditions

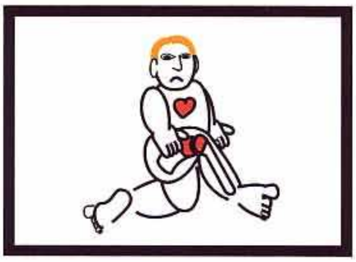


Cold conditions

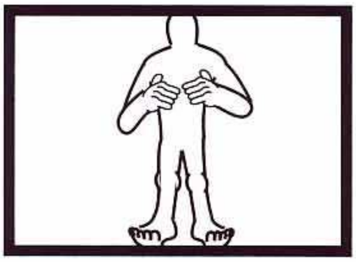
It is unknown why some people make cold auto - antibodies. When exposed to the cold, these IgM 'grab' his RBC's and activate complement. They detach once the temperature returns to normal.

COULD OUR HORMONES HELP TRIGGER AUTOIMMUNITY?

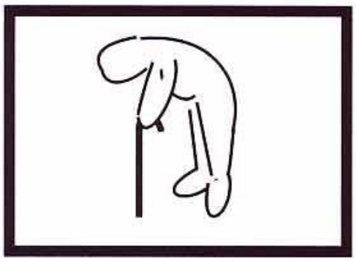
Hormones will alter the shape of our body during our lifetime. So it is possible that for a few people, their immune systems, could 'see' a changed body part as foreign and attack it.



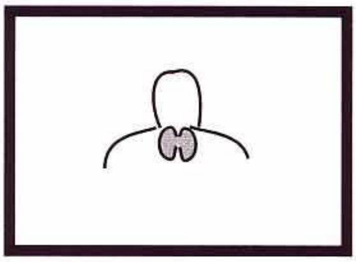
Rheumatic heart disease is most common in children and adolescents.



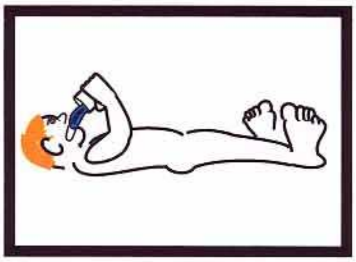
Rheumatoid arthritis most frequently appears in women between 30 and 40.



Ankylosing spondylitis is 8 times more common in men than women.

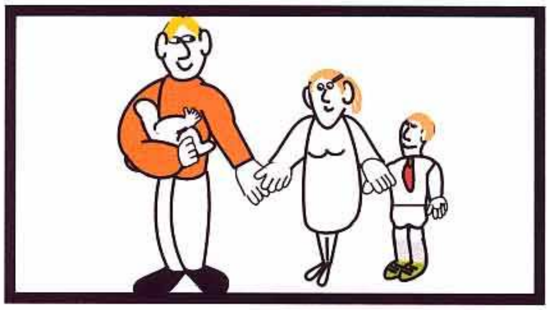


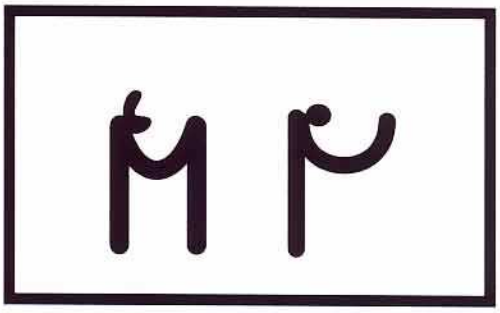
With graves' disease, the highest incidence is in women over 40.



Insulin-dependant diabetes is much less likely to start after the age of 30.

AUTOIMMUNE DISEASES OFTEN APPEAR TO 'RUN' IN FAMILIES





Genes from our parents allow family characteristics like hair colour, to be passed onto the following generation.

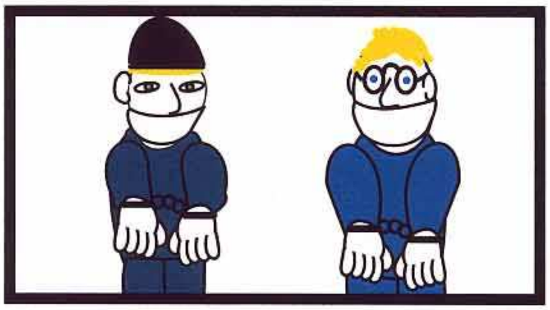
We inherit subtle shape variations at the top of the 'attack' and 'defence' proteins, like those shown above.

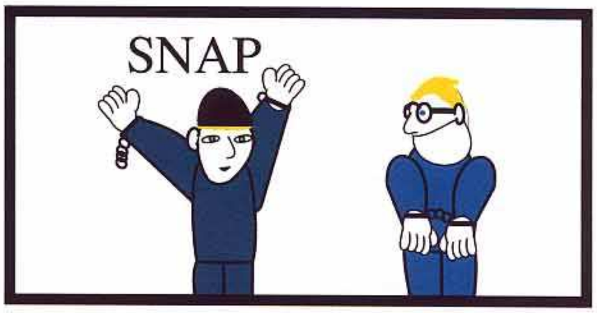
Inherited shape variations at the top of the 'attack' and 'defence' proteins are covered in much greater detail in chapter 11 (see page 221).

A NON-INFECTED CELL IS ATTACKED!

We inherit certain shape variations to our 'attack' and 'defence' proteins. Therefore, some people could be at risk if an immune cell mistakes a non-infected cell for an infected one. This might follow a viral infection (cross-reaction).

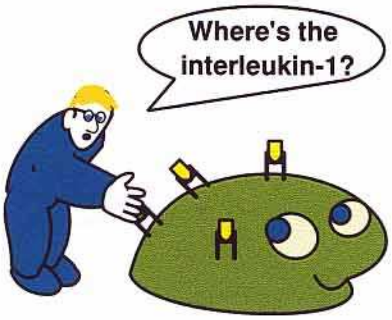
ANERGY





Anergy refers to those mature T cells which appear to have been inactivated, possibly because they had the potential of harming the host.

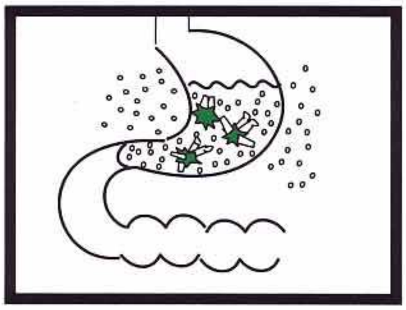
It is likely that we all have a few of these T cells. So if something was to reactivate one or more of these cells, then this could initiate an autoimmune disorder.



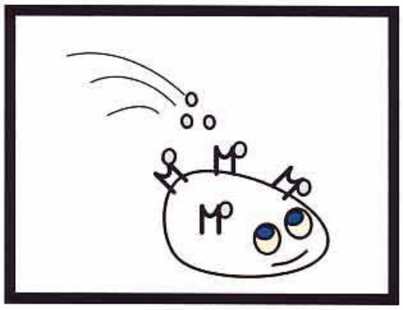
One theory postulates, that if a T cell's 'hand' fits material expressed at a cell's surface, but a second signal is then not received (see page 88), the T cell becomes inactivated.

COULD ENTEROTOXINS TRIGGER AUTOIMMUNITY?

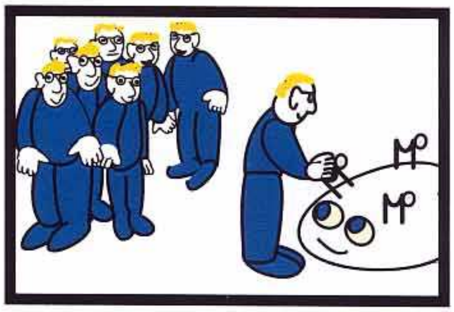
Enterotxins are waste, produced by bacteria that can harm us.



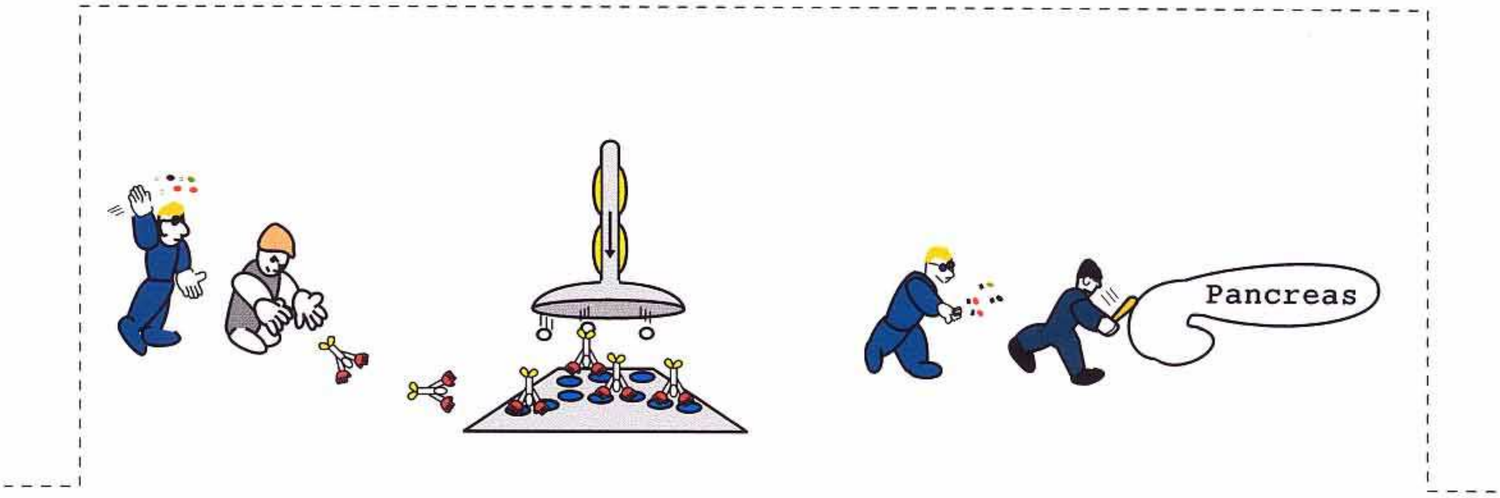
This person has just eaten some contaminated food laced with enterotoxins.



The enterotoxins are soon attaching abnormally onto the 'attack' proteins .

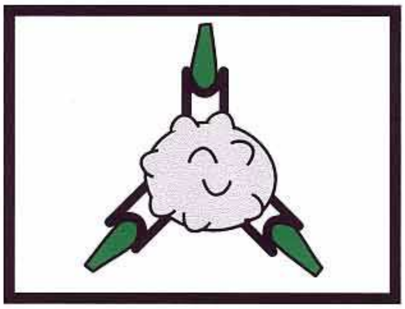


Many more T helpers than normal will now be stimulated (see page 101).



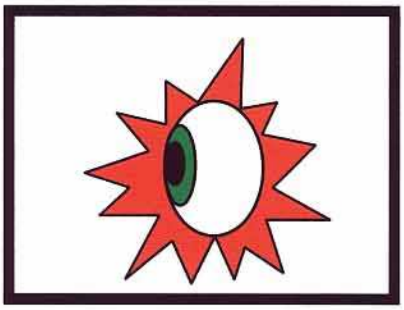
It is possible that something like enterotoxins, could reactivate T cells, which had been inactivated (anergised). This could then lead to an autoimmune disorder such as myasthenia gravis.

OTHER FACTORS WHICH COULD TRIGGER AUTOIMMUNITY



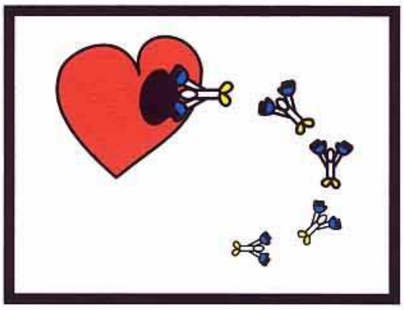
Normally, a virally infected cell expresses viral particles attached to 'defence' proteins. These foreign proteins will be detected by a T cytotoxic cell which will then kill the infected cell (see page 113).

But if a virally infected cell was to express viral particles attached to 'attack' proteins, then an abnormal T helper response could be triggered (see page 80).



Normally, immune cells are prevented from entering certain parts of the body, such as the eye.

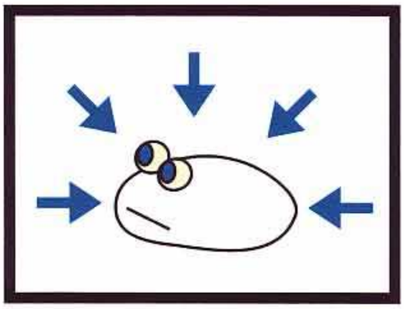
But when immune cells do gain access to these 'hidden' (sequested) areas of the body, the part will be 'seen' as foreign and attacked.



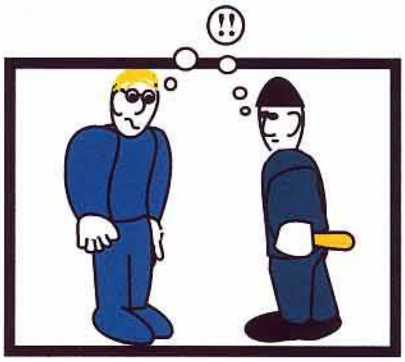
Could an injured (damaged) part of the body be at risk from an immune assult, due to changes in its physical appearance?

This is possible. After a heart attack, it has been known for antibodies to be produced against necrotic heart muscle.

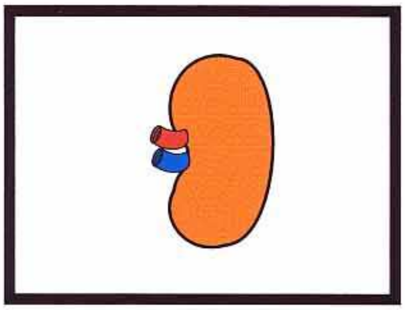
TREATMENTS FOR AUTOIMMUNE DISEASES



Steroids prevent the release of inflammatory mediators from mast cells and neutrophils.

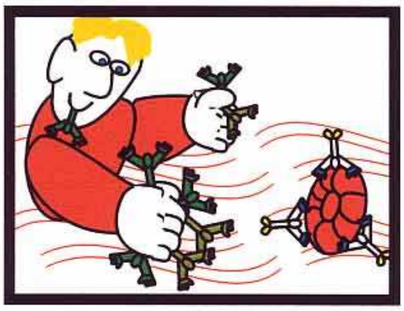


Cytotoxic drugs (ie azathioprine) work by incapacitating the T cells.



The spleen contains macrophages which will 'eat' any host cell coated in antibodies entering it.

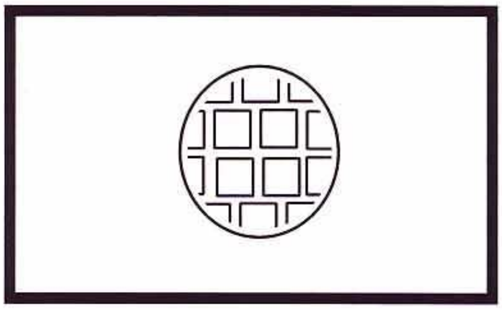
So by removing the spleen, the rate at which these coated cells are removed, is greatly reduced.

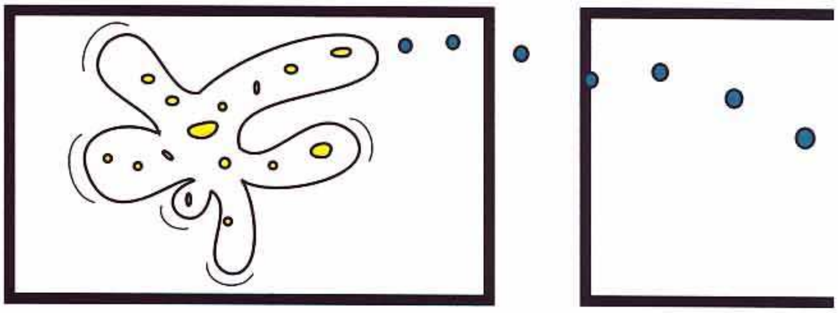


By injecting a large number of antibodies, certain autoimmune conditions, will improve for a while. These occupy the macrophages so that they ignore any host cell coated in auto-antibodies, until all the foreign antibodies have been removed.

CHAPTER TEN

CANCER





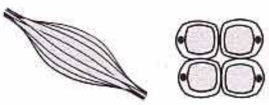
Benign tumours grow slowly and have a regular shape and capsule. But they can become large and so compress things like blood vessels.

Malignant tumours grow rapidly. They have irregular structures, invade adjoining tissues and often release metastases.

Easy reading

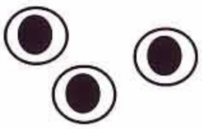
Technical information

WHERE SOME COMMON TYPES OF CANCERS ORIGINATE FROM



Sarcomas...

develop from fat and muscle cells.

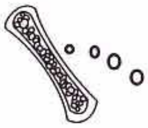


Lymphomas...

Cancerous lymphocytes.

Carcinomas...

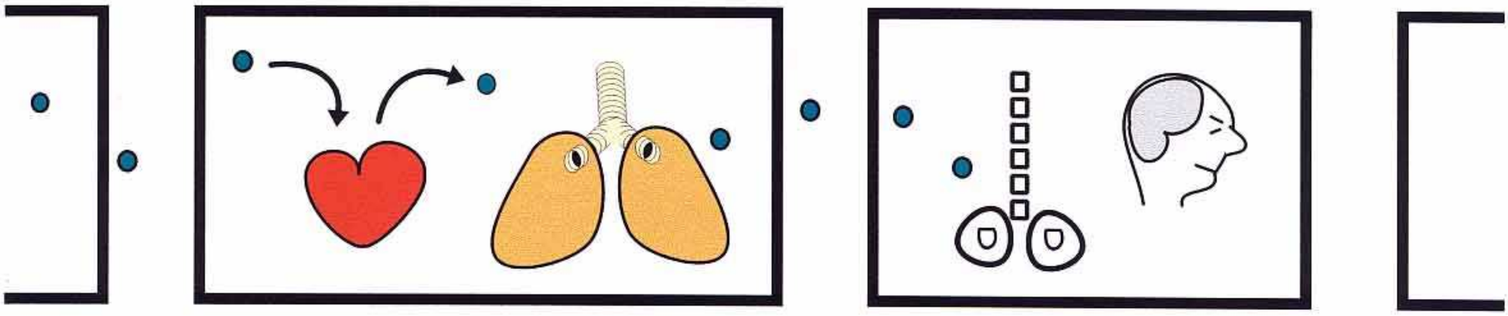
originate from epithelial cells.



Leukaemia..

Malignant blood cells.

SECONDARIES

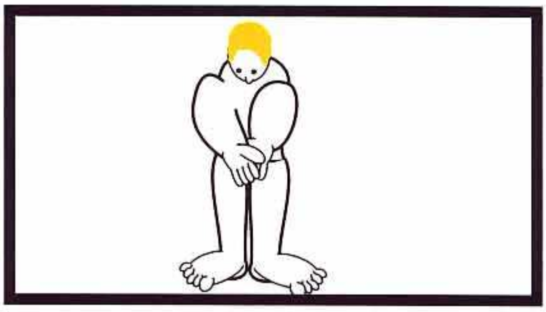


Metastases released into the blood or lymph, are carried to the heart and then in to the lungs, where they may become trapped.

Metastases do not get trapped in the heart, because there are no intricate channels, only 4 large chambers.

Or they travel onto other parts of the body, like the brain or bones and develop there.

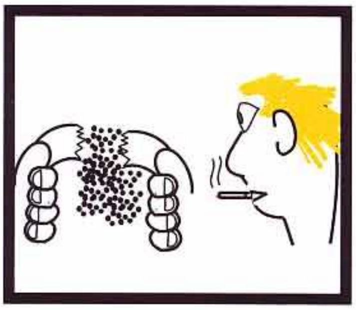
Metastases become trapped in capillary networks due to their intricate, meandering channels.



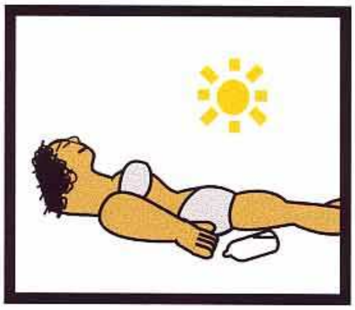
However, with cancer of the prostate, metastases from this tumour frequently become lodged in the patient's bones.

It appears that when some tumours turn malignant, the metastases find it easier to attach and then develop into a secondary, at specific sites in the body.

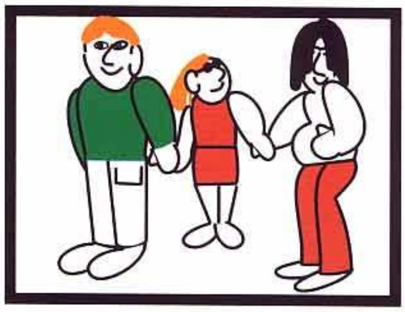
SOME LIKELY CAUSES OF CANCER



Chemicals such as soot, tobacco tar and asbestos.

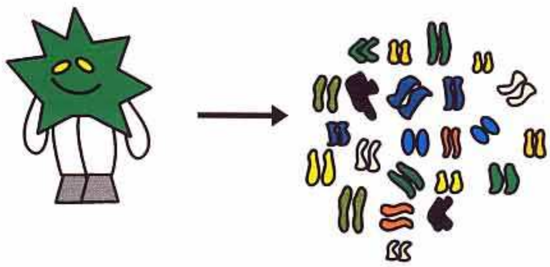


Physical damage due to X rays, UV light etc.



Inherited genetic defects may be the reason many cancers appear to 'run' in families.

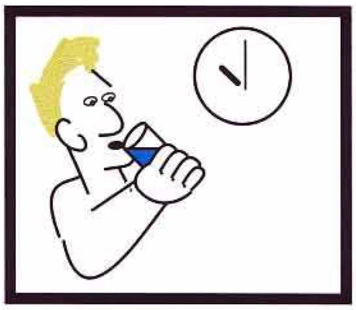
Eating too little fresh fruit, vegetables and roughage, appears to increase the chances of acquiring certain cancer.



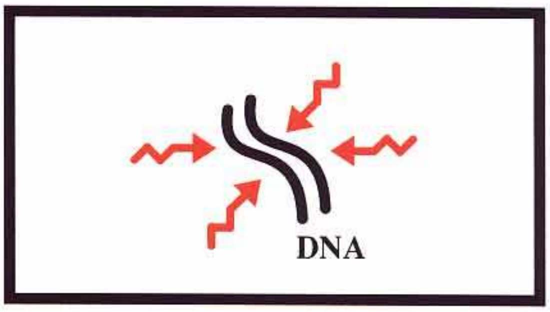
Viral genes acquired following an infection, could turn a cell malignant, by affecting the processes involved in random gene rearrangemnt (see page 121).

LOOKING FOR SECONDARIES

Almost overnight, Paul finds that he can't walk and has to go to hospital to find out what's wrong.

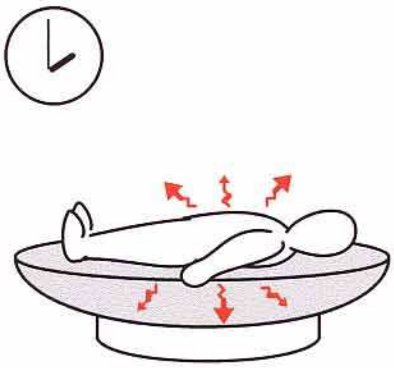


Here he drinks a solution containing chemicals, which will be absorbed by any replicating cell.

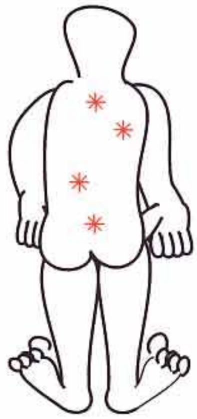


As cancer cells replicate faster than normal cells, they will absorb more of these chemicals, which were labelled with a small amount of radioactivity.

A FEW HOURS LATER

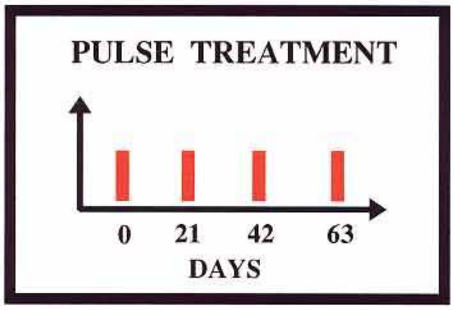


Paul lies on a receiver, which will pick up traces of radio-activity emitting from him.

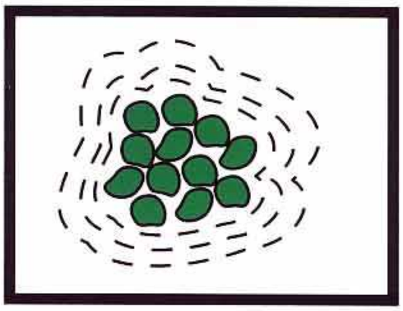


Any tumour will now appear as a 'hot spot', having absorbed more of the labelled material.

ANTI - CANCER DRUGS (ie CHEMOTHERAPY)



Because anti-cancer drugs affect all replicating cells, treatments are spaced out to allow normal cells time to recover.



Tumour cells are generally less resillient and hopefully have insuffient time to recover and die.

Often the most distressing side effects for the patient are the loss of hair, vomiting and diarrhoea.

The worst side effects of chemotherapy are on parts of the body made up of cells that replicate quickly.

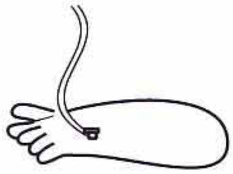
The lining of the gut → Vomiting Diarrhoea

Hair folicles → Baldness

A foetus → Potentially fatal

Sperm → Possible infertility

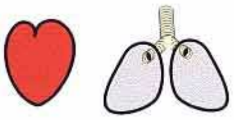
OTHER SIDE EFFECTS OF CHEMOTHERAPY



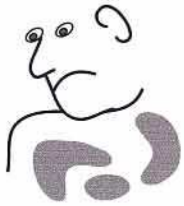
Anti-cancer drugs are very toxic and can cause a lot of damage if they happen to leak into the tissues at the site of the infusion.

Cytotoxic drugs can cause uric acid deposits to build up in the urinary tract, so lots of water must be consumed to flush away these impurities.

Because many anti-cancer drugs are toxic to nerves, peripheral neuritis is sometimes experienced in the hands and feet.



Heart and lung irritation are sometimes experienced.



Skin pigmentation may appear, following the use of steroids.

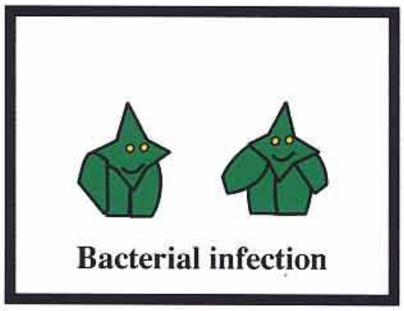
HOW SOME CYTOTOXIC DRUGS WORK

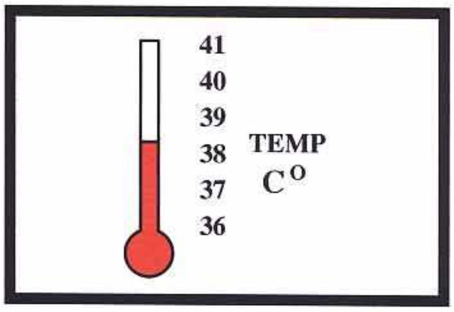
Alkylates (ie Cyclophosphamide), damage DNA so that cell division is prevented.

Vinca alkaloids (ie Vincristine), disrupt microtubules during chromosomal replication.

Antimetabolites (ie Methotrexate), attach to enzymes and so prevent normal cell division.

INFECTIONS IN THE IMMUNOSUPPRESSED PATIENT



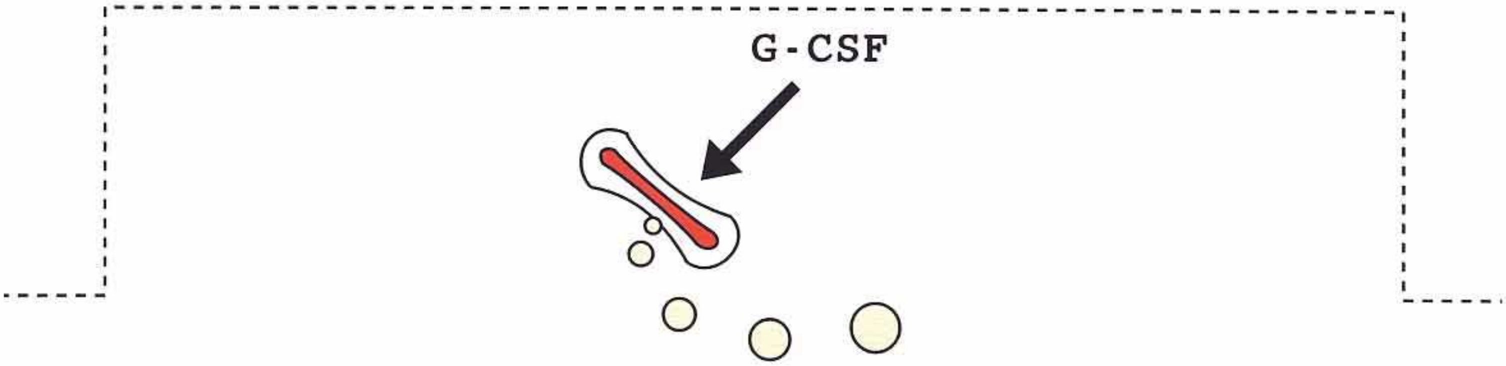


As cytotoxic drugs affect all replicating cells in the body, the immune system is frequently affected.

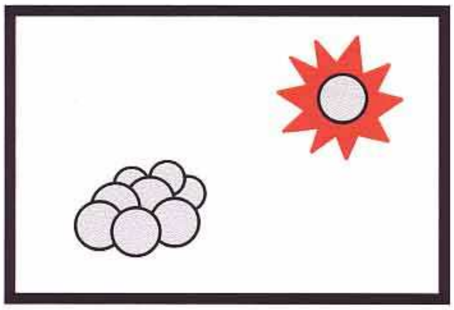
The bone marrow is often unable to release sufficient numbers of neutrophils to combat an infection.

Hence, patients undergoing anti-cancer treatment require daily temperature readings to detect early signs of an infection.

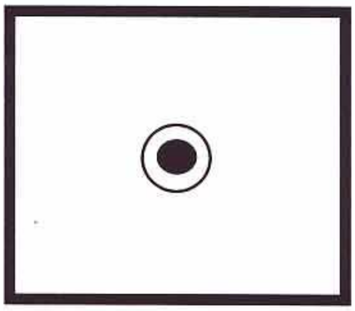
These patients often have a reduced number of neutrophils (ie they are neutrophenic). So at the first signs of an infection (such as a raised temperature), antibiotic treatment is commenced.



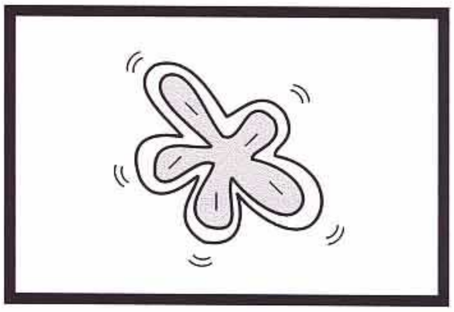
Severely immuno-depressed patients are at risk from overwhelming infections. So they may be given bone marrow stimulants, such as granulocyte colony-stimulating factor or G-CSF (see page 90).



A normal cell needs positive signals from adjoining cells, as it will die if kept in isolation.

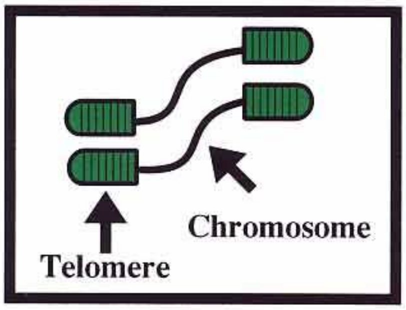


But isolated cancer cells can survive indefinitely and become 'immortal'.



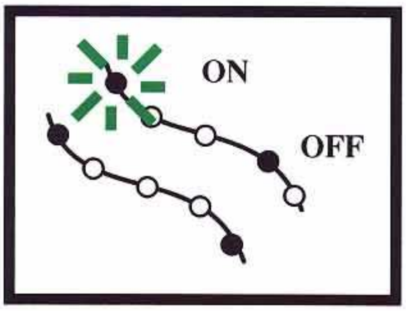
Malignant cells can also 'ignore' negative growth signals as they invade adjoining tissues.

CELLS OUT OF CONTROL

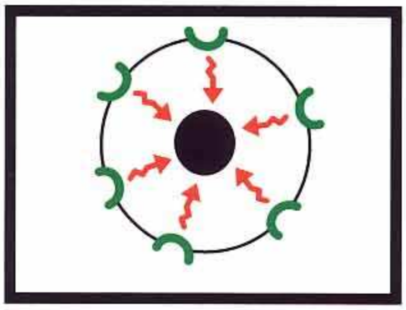


Chromosomes have end pieces called "telomeres". These shorten each time a chromosome is copied. As a telomere can only shorten to a certain point, a normal cell is unable to replicate indefinitely.

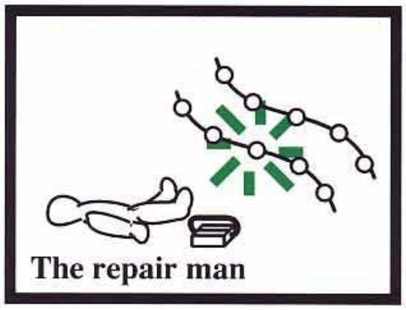
All tumour cells acquire enzymes which add material to telomeres. This stops the telomeres shortening when the chromosomes are copied, so that the cell can now replicate indefinitely.



Along any chromosome, there are many ON and OFF genes. In cancer cells, an ON gene (oncogene) could become jammed on, or an OFF gene (tumour suppressor gene) may have failed to work.

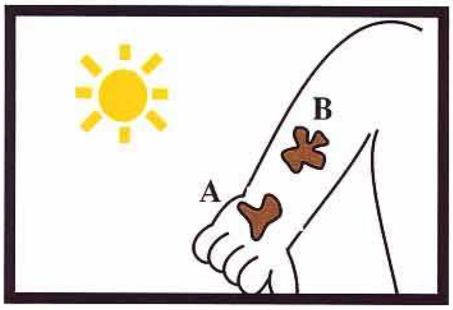


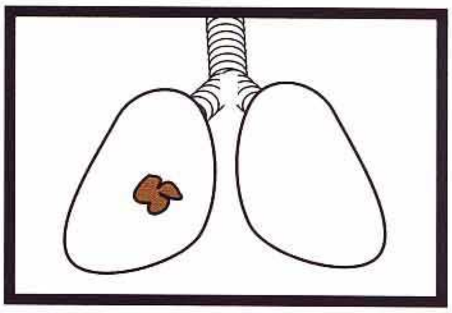
Growth receptors on the surface of a cell could malfunction and start to fire impulses to the nucleus, without any growth factors being attached.



Some cells appear to lose the ability to repair damage sustained to a chromosome and the unrepaired genes could now turn the cell cancerous.

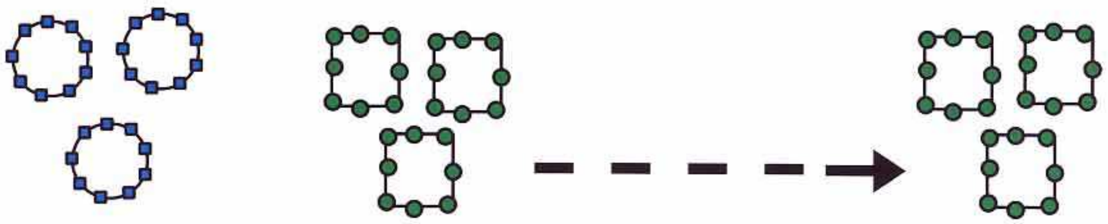
RANDOM GENE MUTATION





These skin cancers were caused by the sun, randomly damaging genes inside 2 skin cells.

Some time later, a secondary, originating from tumour B, has developed in the lungs.



Cells in cancer A

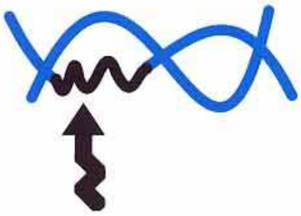
Cells in cancer B

Cells in the lung secondary

Random gene mutation means that cells in the 2 skin cancers are very different.

But cells in the secondary will be identical to those found in the primary.

DANGEROUS GENES?



Sunlight, X rays and chemicals can all damage our DNA (genes) and this might then turn a cell cancerous.

Inherited genetic defects could cause a cell to malfunction.

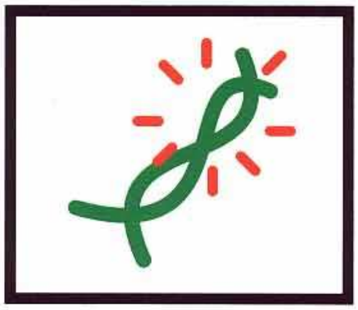
Viral genes incorporated onto a human chromosome, may deregulate the normal genes and trigger uncontrolled cell division.

Something might cause a malfunction to the enzymes in the nucleus and this initiates uncontroled cell division.

SILENT GENES

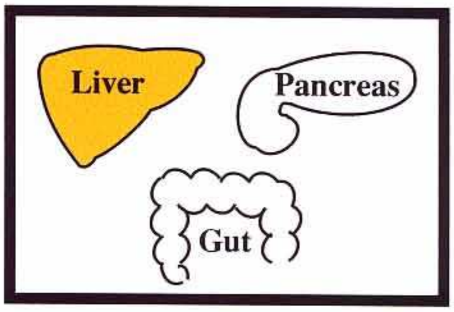
It is possible that an external factor, could accidentally activate a gene which is not normally used and this then triggers unrestricted cell division.

ONCOFOETAL GENES



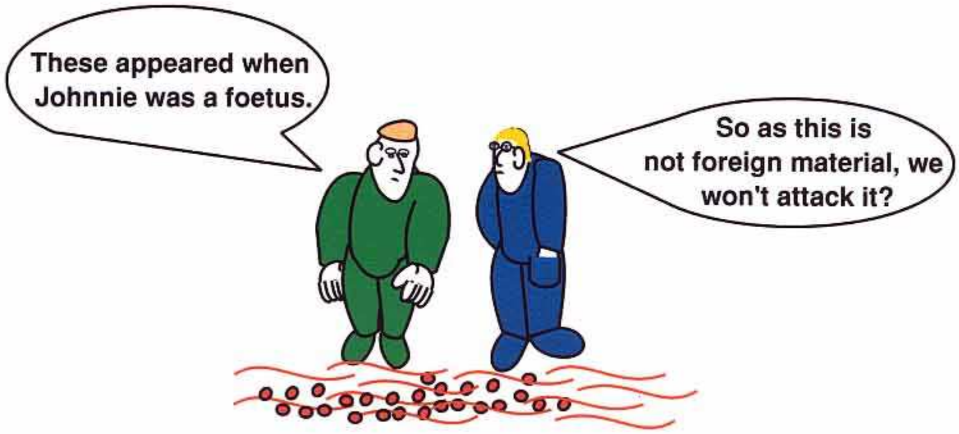
Certain genes inside a pregnant mother and her foetus, start to work.

Alpha - fetoprotein (AFP) soon appears in both the foetal and maternal blood.



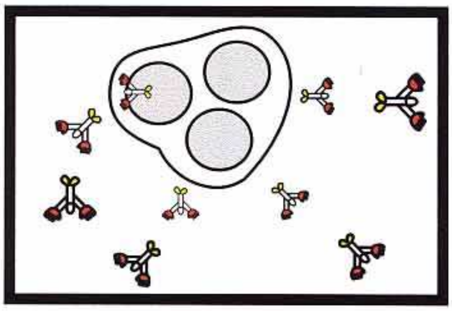
Carcinoembryonic antigen (CEA) coats the surface of certain foetal organs like the gut and pancreas.

After the birth, the oncofoetal genes are switched off, so that both AFP and CEA soon disappear from inside the mother and her newborn baby.

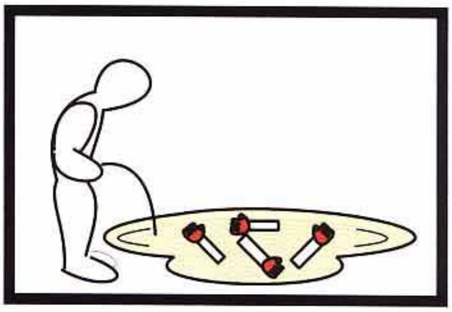


But both sets of genes can be turned back on. AFP is released by some liver and testicular cancers. CEA reappears in people with certain bowel cancers, emphysema and those who smoke or drink heavily.

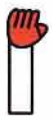
BENCE - JONES PROTEINS



Myelomas which develop from malignant plasma cells, release many identical antibodies.



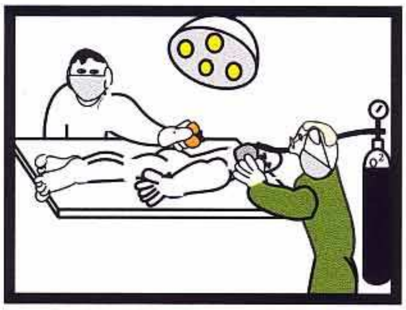
Often, antibody light chains (ie their 'arms') now start to appear in the patient's urine.



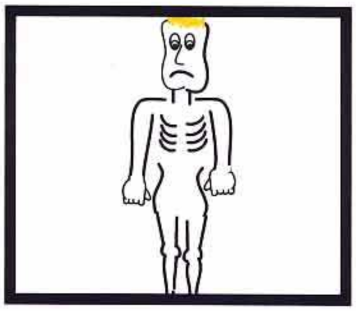
When light chains appear in the urine, they are called "Bence-Jones proteins".

DO VIRUSES CAUSE CANCER?

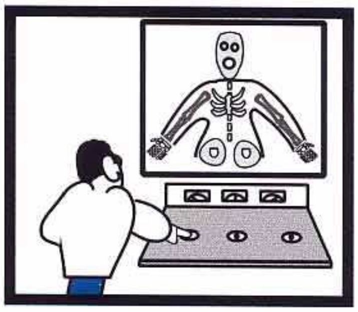
Before answering this, remember that T cells are responsible for eliminating virally infected cells.



To stop a transplant from being rejected, a patient's T cells must be suppressed.

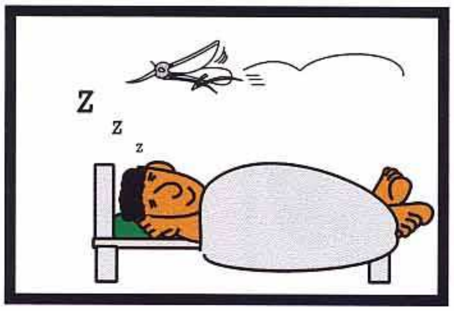


People with AIDS have few, if any, T helper cells.

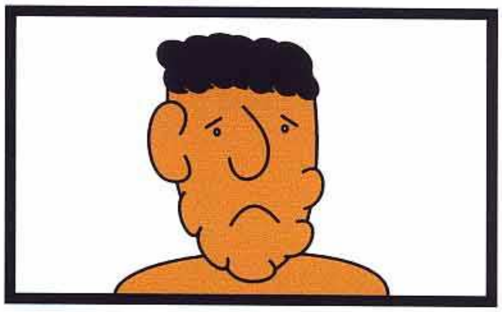


Radiotherapy can badly deplete T cell numbers.

Although there is NO increased incidence of the commonest cancers in these patients (ie lung, breast and gut tumours), there is a 50 times increase in the incidence of lymphomas.



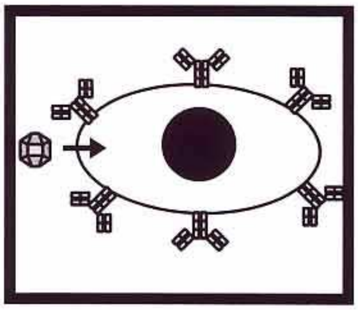
In parts of West Africa, a certain strain of malaria is endemic.

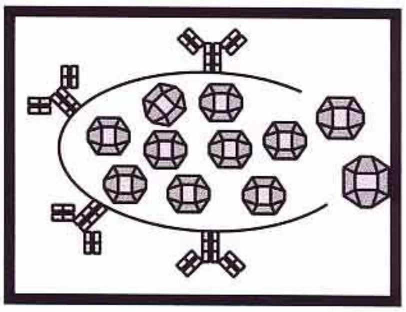


And here there is a high incidence of young people suffering from Burkitt's lymphoma.

This strain of malarial, appears to deplete T cell numbers. This could then account for the high incidence of Burkitt's lymphomas in West Afican young people.

LYMPHOMAS AND THE IMMUNOSUPRESSED PATIENT





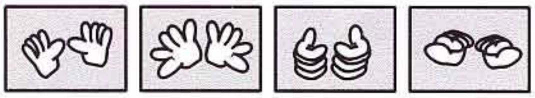
The Epstein-Barr virus routinely infects most B lymphocytes.

But if the virus then starts to replicate itself, the infected cell is eradicated.

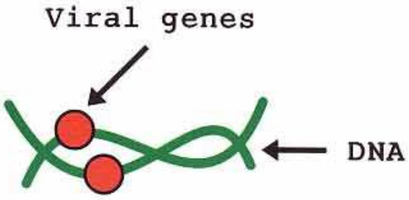
So if the T cells were to be removed, the virus could now replicate unhindered.

Although a lack of T cells would allow a virus to replicate unhindered, how could this now cause the infected B cell to become cancerous?

WHAT MAKES LYMPHOCYTES DIFFERENT TO OTHER CELLS?

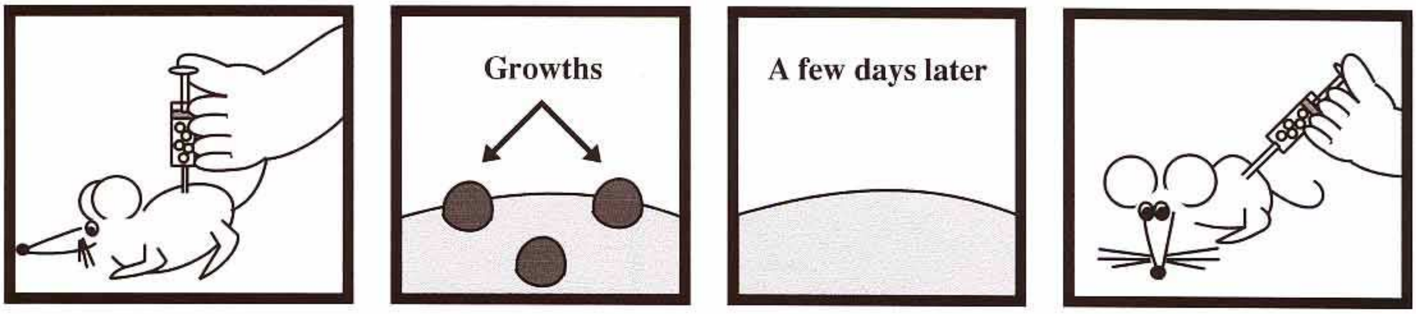


Each mature lymphocyte has a unique 'hand' shape, due to recombinase enzymes.



If the virus can now replicate unhindered, this could affect these enzymes, turning the cell cancerous.

IS THERE AN ANTI - TUMOUR MEMORY?



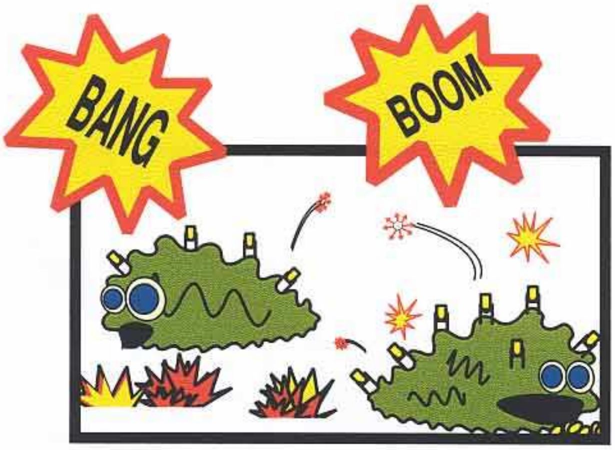
Cancer cells from a genetically identical mouse are injected.

Skin growths appear for a few days and then vanish.

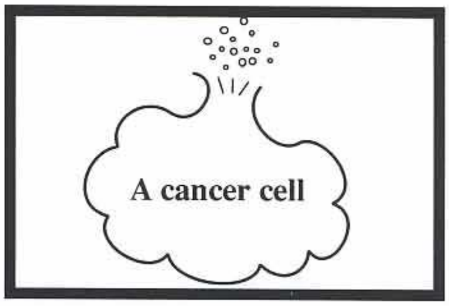
But when more of these cancer cells are injected, no new growths appear.

This indicates that the immune system could have an anti - tumour memory.

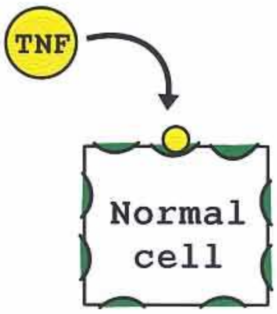
TUMOUR NECROSIS FACTOR (TNF)



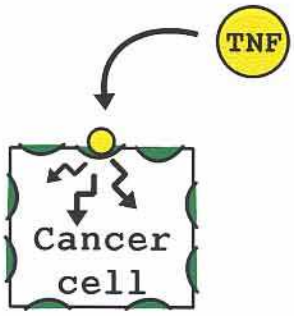
Whenever macrophages are activated, they release a cocktail of chemicals including tumour necrosis factor.



Tumour necrosis factor has a range of actions, one of which causes some cancer cells to die.

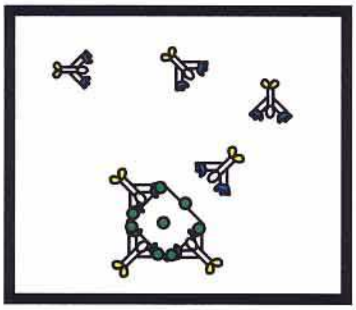


Most cells have receptors for TNF. If TNF binds to these, toxic chemicals are produced inside the cell.

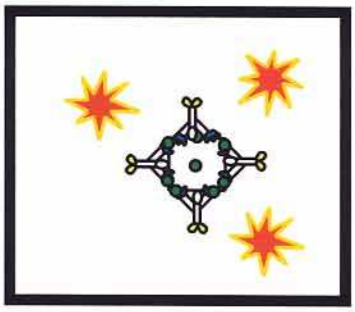


Normal cells deactivate these, whereas some cancer cells seem to lose this ability and die.

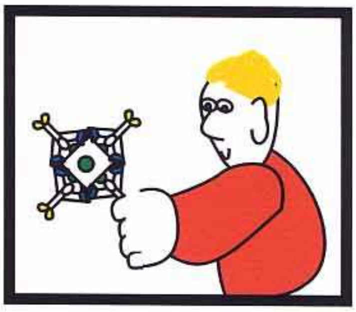
HOW ANTIBODIES MAY HELP FIGHT CANCER?



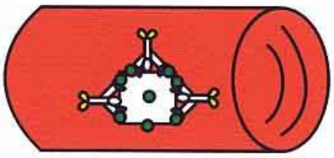
First, antibodies must attach onto the cancer.



Complement activation could now follow.

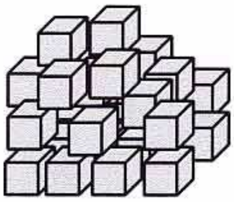


Or, the cell is eliminated by an immune cell.

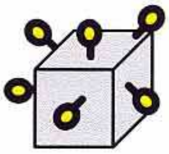


If antibodies manage to coat the surface of a metastase in the blood, the cancerous cell may be prevented from attaching onto the side of a capillary and developing into a secondary (see page 196).

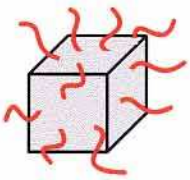
HOW TUMOURS MAY EVADE IMMUNE ELIMINATION



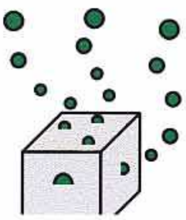
The rapid growth associated with many cancers could overwhelm the immune system.



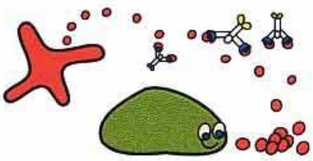
Some tumours express more glycocalyx molecules than normal cells and this could 'hide' the cancer from the immune system.



Other tumours coat themselves in fibrin, which could 'mask' them from the host's immune system.



Many tumours release transforming growth factor. Because this affects macrophages and lymphocytes, their anti-cancer capabilities may be affected.

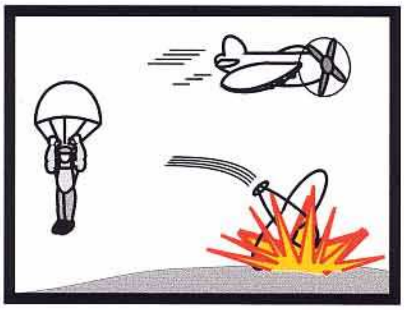


A tumour could protect itself by releasing 'blocking factors', which occupy the immune system and so allow it to remain untouched.

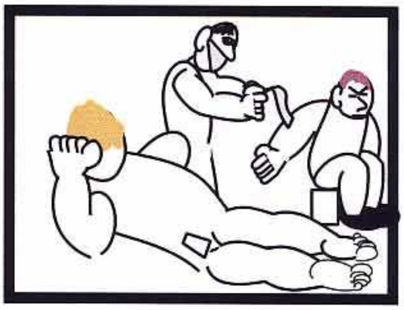
CHAPTER ELEVEN

TRANSPLANTS

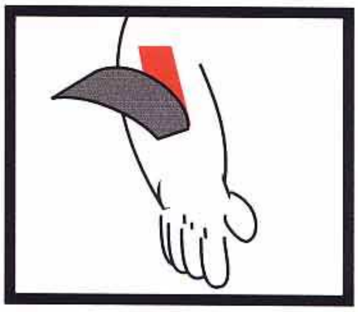
TRANSPLANTATION CAME OF AGE DURING WORLD WAR TWO



Many of the badly burned pilots required skin grafts.



At first, skin was taken from any donor.



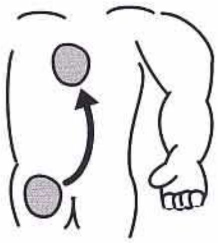
But it invariably peeled away after a few days.

Easy reading

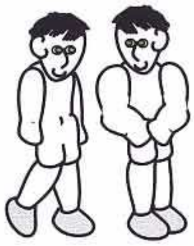
Technical information

Today, organ transplants are much more successful through the advent of many anti-rejection drugs and modern tests.

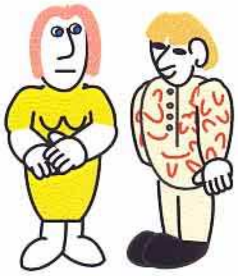
TRANSPLANT TERMINOLOGY



Autograft: When tissue (ie skin), is moved from one part of the body to another site.



Syngraft: An organ donated from an identical twin.



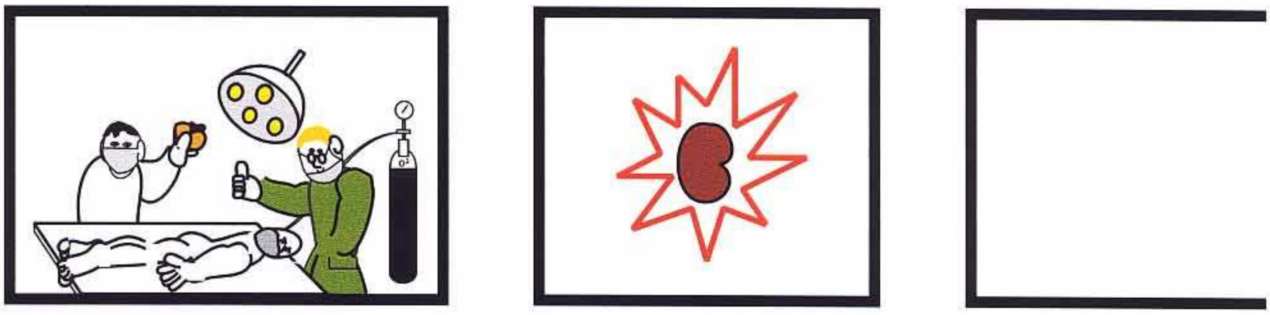
Allograft: An organ which came from a genetically different person.

Xenograft: This is an organ taken from another species (ie a pig).

A donor is the person who gives an organ and a recipient is the person who receives it.

ACUTE ORGAN REJECTION

This is what would almost invariably occur, if modern drugs and tests were not available.

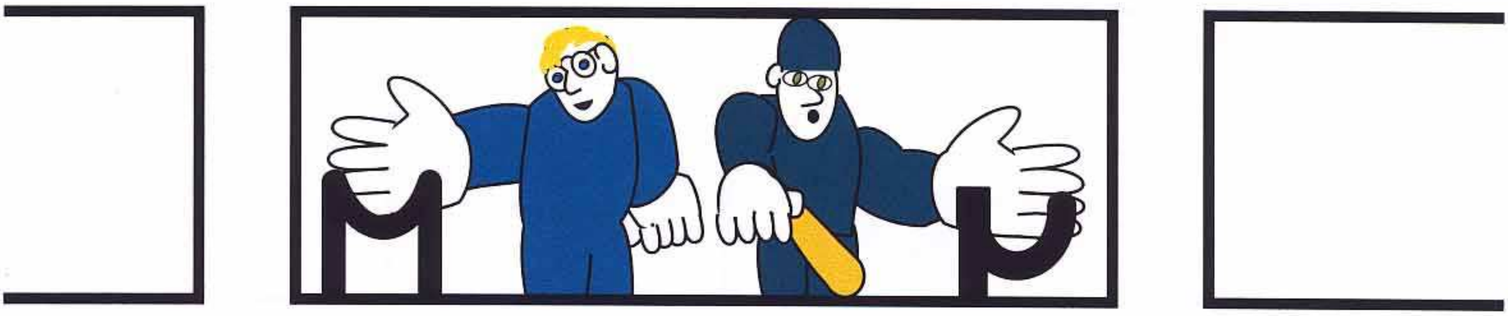


This patient is just about to receive a kidney transplant.

10 to 14 days later, it starts to fail and dies.

T cells entering the graft, destroy it.

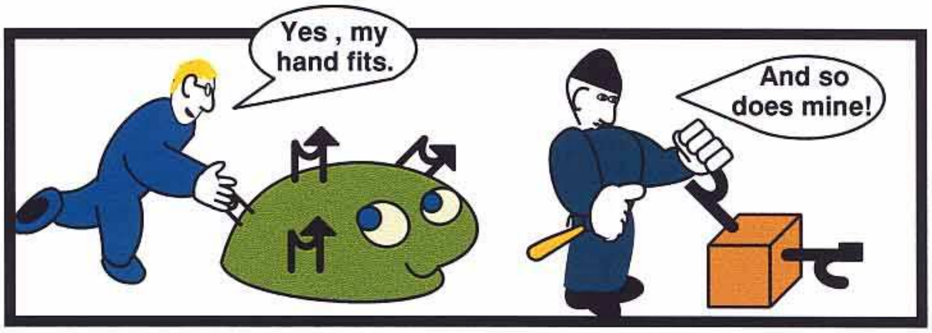
SO WHY WOULD T CELLS ATTACK A HEALTHY GRAFT?



T cells entering a graft, would find that their 'hands' fitted the 'attack' and 'defence' proteins. However no foreign material is attached to them (see pages 85 and 115).

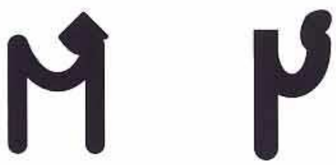
There are actually small shape variations at the top of the 'attack' and 'defence' proteins, inherited from our parents. How we acquire these is shown on page 240.

INSIDE THE GRAFT



Both T helper and T cytotoxic cells mistakenly 'believe' that they are confronted with an infection which must be eliminated.

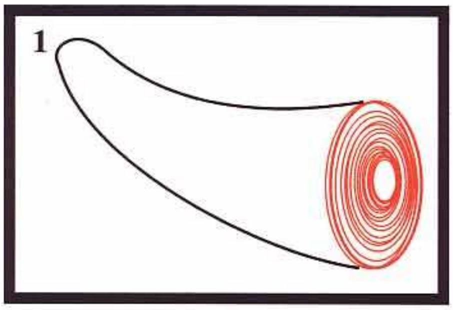
Inside the transplant are these shaped 'attack' and 'defence' proteins.

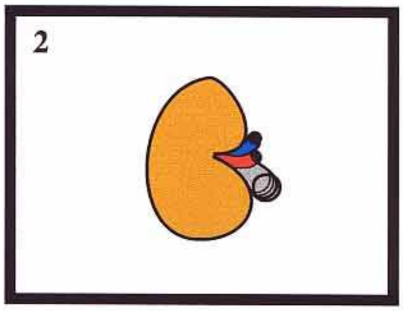


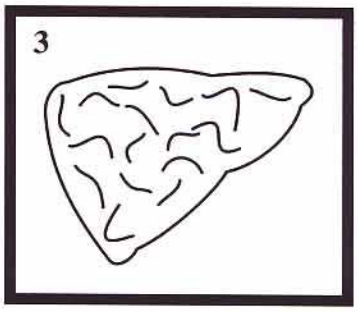
But the recipient has these shaped 'attack and 'defence' proteins.

CHRONIC ORGAN REJECTION

**Years after receiving a transplant, it can gradually fail.
This is usually due to one or more causes:-**



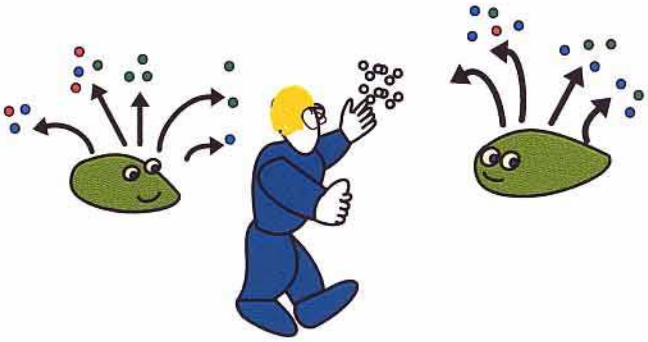




Inflammatory damage to the arterioles and / or occlusion of the graft's blood vessels.

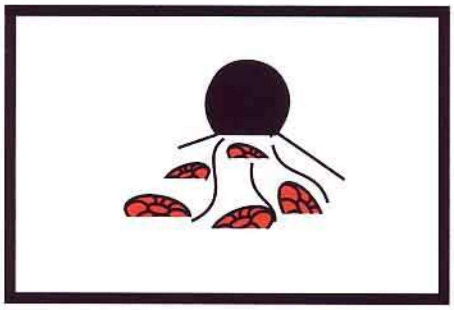
Thickening of the glomerular basement membrane inside a kidney transplant.

Generalised fibrosis inside the transplant.

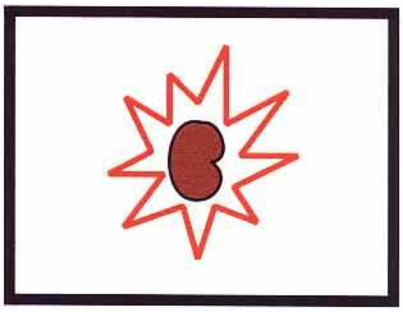


The above could result from T helper cells stimulating the resident macrophages into releasing growth factors, over a prolonged period of time.

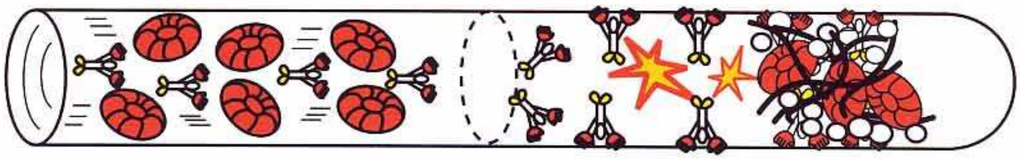
HYPERACUTE ORGAN REJECTION



As the operation finishes, blood starts flowing into the transplant.



Minutes later, the graft has been rejected and is dead.



Anti-graft antibodies enter the transplant and 'grab' the sides of its blood vessels.

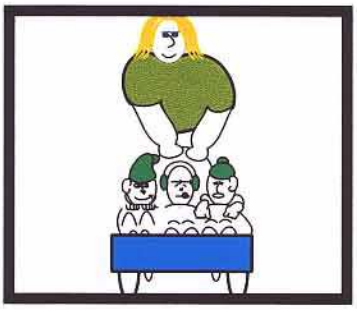
↓

Complement is activated.

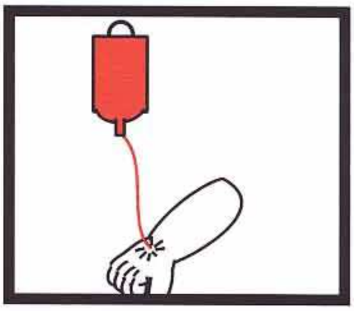
↓

This causes blood clots to form inside the graft and occlude its arteries.

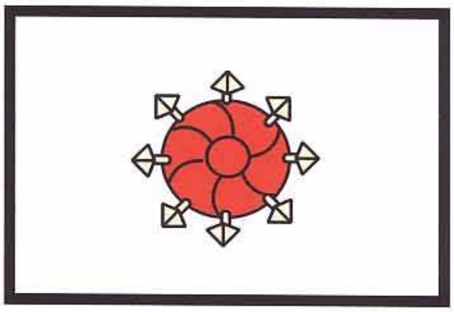
WHO MAY HAVE ANTI - GRAFT ANTIBODIES IN THEIR BLOOD?



Mothers who have given birth to a large number of children.



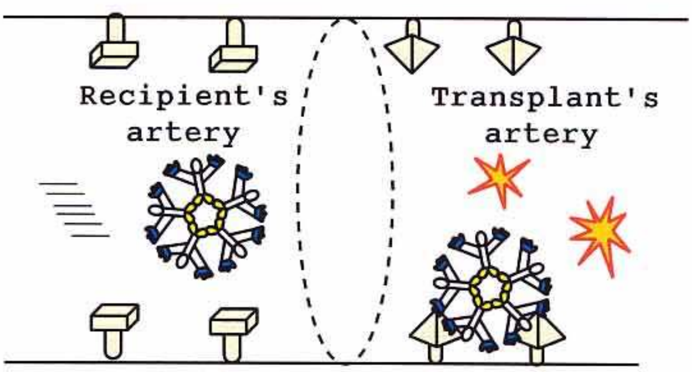
People who have been given a large number of blood transfusions.



Receiving a transplant from a donor with an incompatible blood group (see page 226).

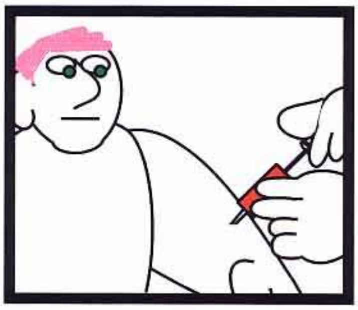
If you reject a transplant from someone (ie skin), then you will not be able to receive a second transplant, like a kidney from the same person. Antibodies with 'hands' fitting their tissue, will now be present.

INCOMPATIBLE ABO BLOOD GROUPS

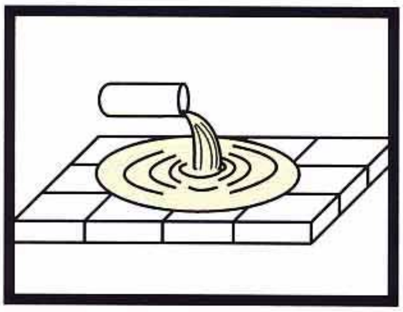


ABO blood group markers (see page 167) also line our blood vessels. Hence a transplant taken from a donor with an incompatible blood group, is doomed from the start.

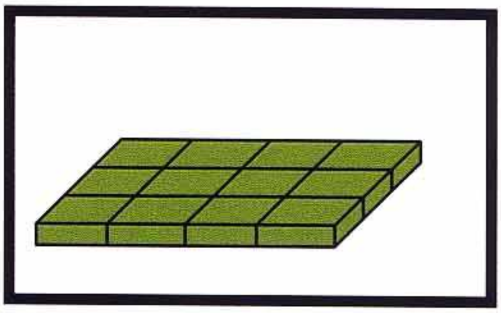
HOW TO DETECT IF SOMEONE HAS ANTI - GRAFT ANTIBODIES IN THEIR BLOOD



Blood is taken from someone who needs a kidney transplant.



Their serum is now applied to a small piece of tissue from the proposed organ.



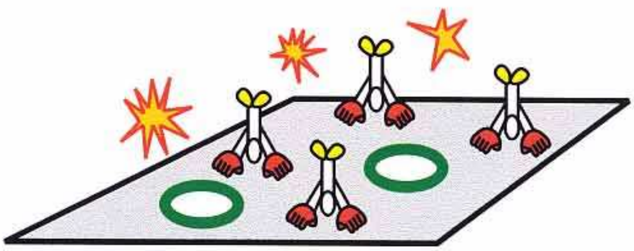
A dye is then applied to the tissue.

↓

If the tissue now turns green, no anti-graft antibodies are present.

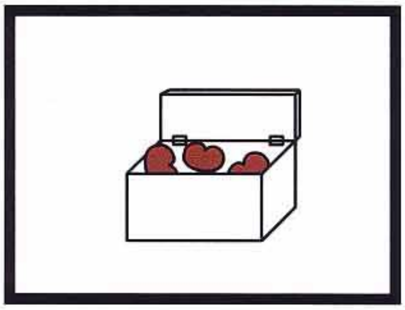
↓

But if the tissue had turned red, it would have shown that anti-graft antibodies were present.

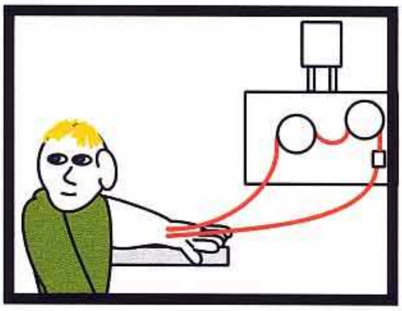


If anti-graft antibodies are present, they will attach onto the tissue sample and activate complement. Holes are punched through its surface (see page 37). The dye can now enter and react with the nuclear material inside and turn the tissue red.

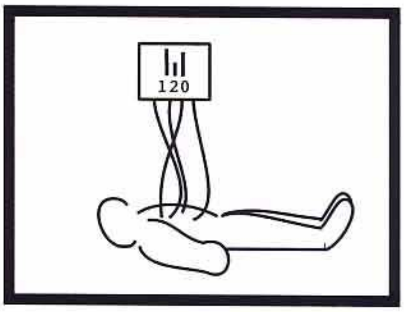
WHY ARE KIDNEYS THE MOST SUCCESSFUL ORGAN TO TRANSPLANT?



Kidneys, unlike other organs, can be stored until a suitable recipient is found.

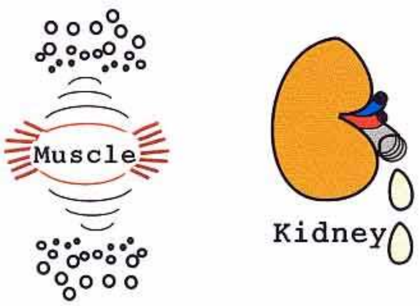


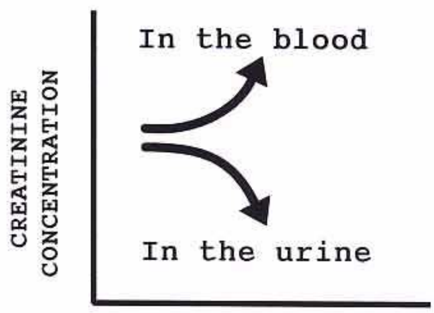
If both kidneys should fail, dialysis can be started until a suitable kidney is found.



But when other organs fail, a patient becomes very ill and needs a transplant quickly.

CREATININE CLEARANCE





Creatinine, a waste product from muscle cells, is excreted in the urine by our kidneys.

So if a transplanted kidney starts to fail, less creatinine is filtered out of the blood.

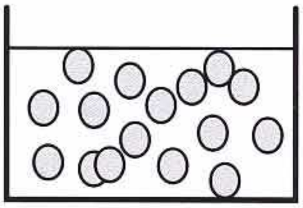
A MIXED LEUCOCYTE REACTION

T cells from the recipient and the proposed transplant are mixed together and left for a few days.

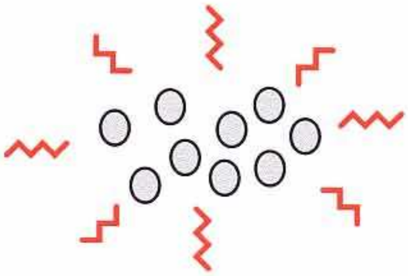
If both sets of cells coexist peacefully, then the transplant should be accepted.

But if a conflict starts, then it is likely that this transplant will be rejected.

HOW TO DETECT IF THE T CELLS ARE ATTACKING EACH OTHER



The T cells are placed in a medium containing radioactive thymidine.

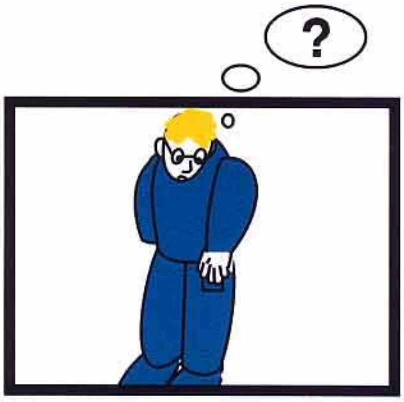


A few days later they are measured for radioactivity.

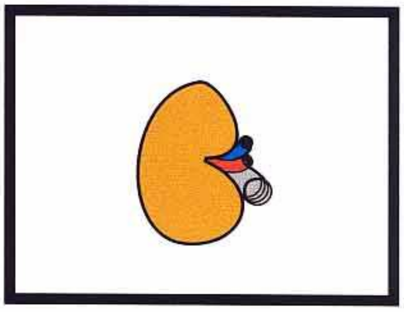
In a conflict, the T cells will start to replicate (see page 115). But to do this they must absorp thymidine.

CYCLOSPORIN

This anti-rejection drug, has significantly lengthened the time a transplant survives.



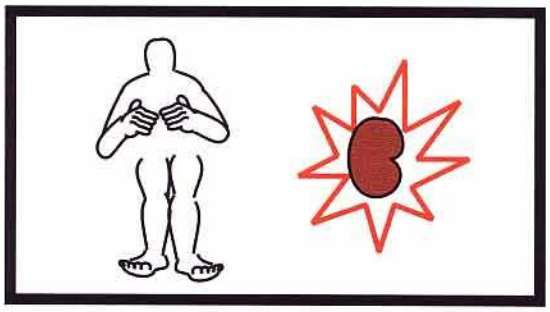
Cyclosporin stops T helper cells releasing factors which would damage a transplant.



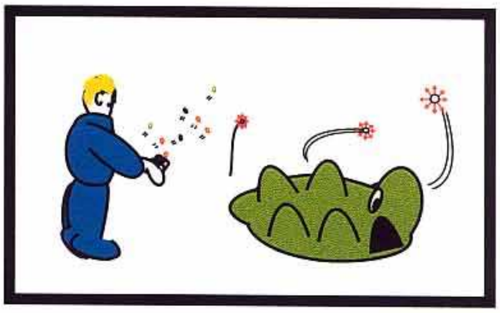
Unfortunately, this drug can be toxic to the kidneys.

Cyclosporin stops gene transcription inside the T helper cells. This prevents them from releasing factors like interleukin-2 and gamma interferon, which would signal the graft's destruction.

AZATHIOPRINE

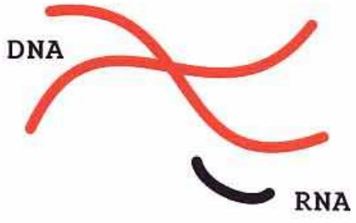


Azathioprine is used in the treatment of certain autoimmune diseases and to help prevent transplant rejection.



It appears to limit the production and discharge of cytokines from macrophages and T helper cells.

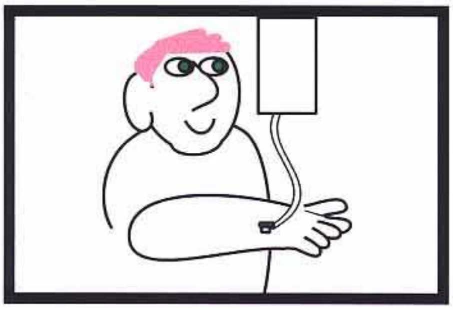
After receiving a transplant, the patient must take immunosuppressive drugs for the rest of their life. Unfortunately this greatly increases the risks of acquiring certain cancers and life-threatening infections. Perhaps a new approach is needed for the 21st century!



Azathioprine, being an antimetabolite, affects RNA synthesis (see page 130).

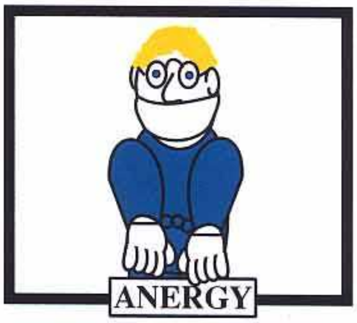
SIMULECT

This recently developed anti-rejection drug, uses monoclonal antibodies (see page 258).

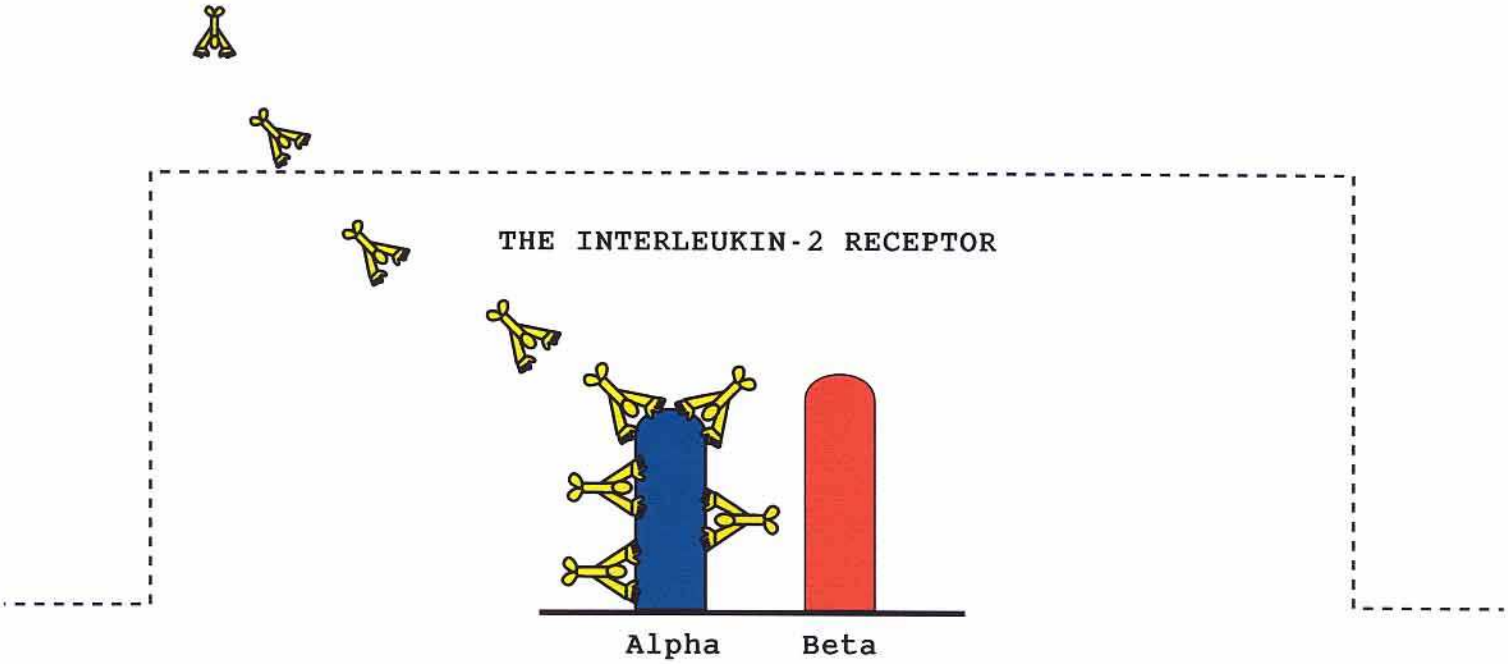


Simulect is given just prior to transplant surgery. It contains antibodies which will attach onto all the patient's T helper cells.

Following surgery, some of the T helper cells now entering the transplant, start to attack it.

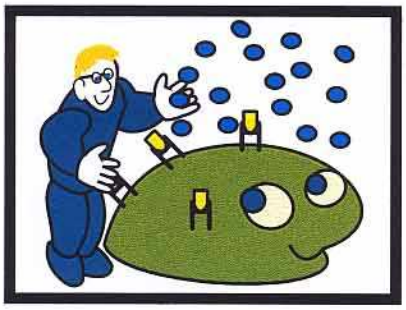


The attached antibodies now take effect. They appear to 'switch off' these T helper cells.

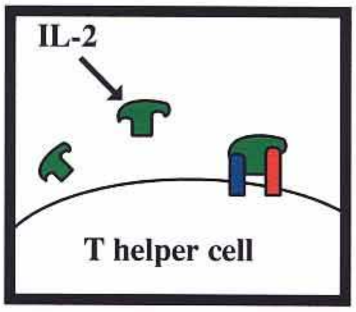


The 'hands' of these antibodies, only fit the alpha chain of the T helper cell's interleukin-2 receptor.

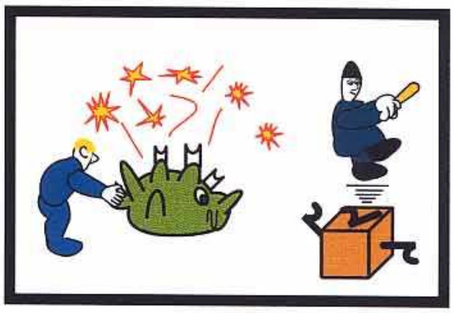
WHY IS THE INTERLEUKIN - 2 RECEPTOR SO IMPORTANT?



This T helper's 'hand' fits and it receives the second signal, interleukin-1 (IL-1).



The T helper will now release interleukin - 2 which must bind onto its interleukin-2 receptor.



Only now can it release the cytokines which will activate any T cells and macrophagses which are close by.

↓

But when antibodies attach onto the alpha receptor, they block the interleukin-2 (IL-2).

↓

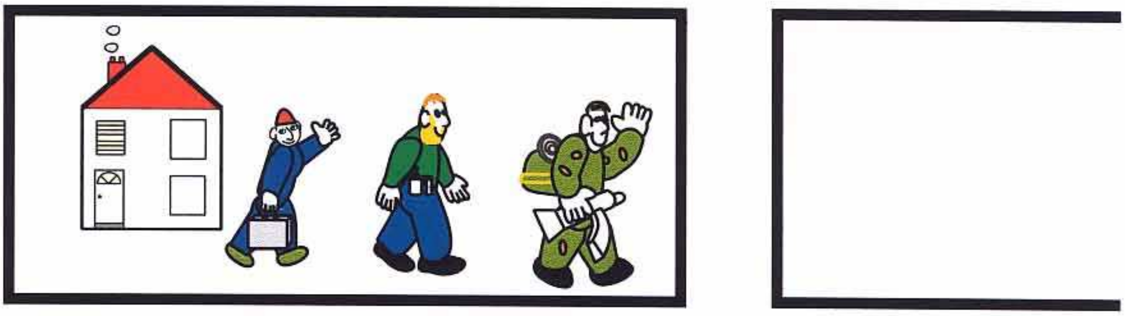
ANERGY

↙ ↘

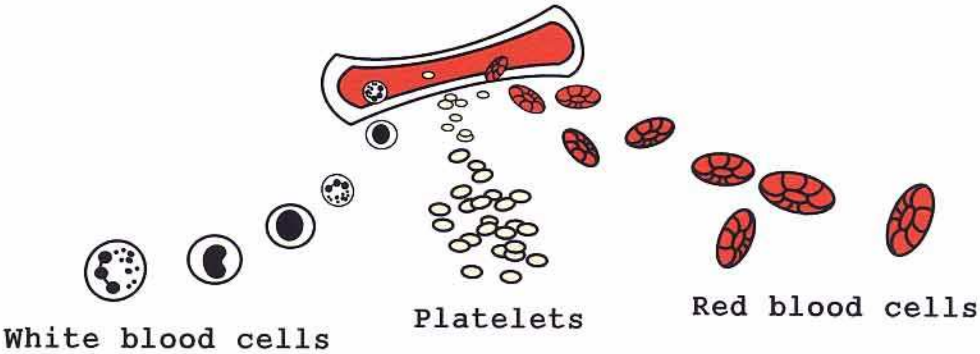
The drug only remains active for about 4 weeks. However, early results indicate that little or no immunosuppression is needed following transplant surgery.

If it is possible to 'switch off' active T helper cells, it might now be possible to cure many autoimmune disorders.

THE BONE MARROW

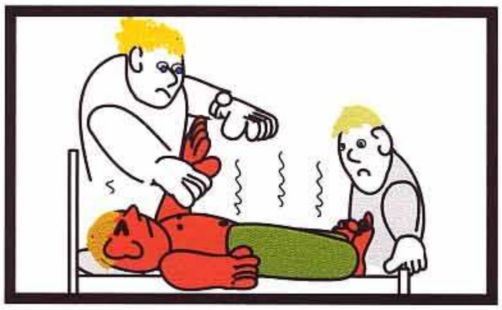


The bone marrow is where blood cells are born and develop, before entering the circulation.



Some of the main factors to appear from the bone marrow, are immune cells like neutrophils, platelets (which enable blood to clot) and red blood cells.

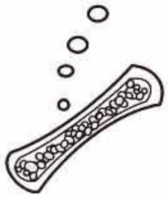
DOCTOR GRAY WAS WORRIED ABOUT JASPER



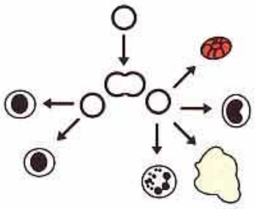
Young Jasper had a variety of symptoms which included a high temperature and bruising.

Sadly, blood and bone marrow samples confirmed that he has leukaemia.

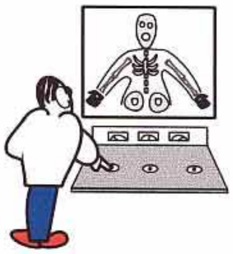
WHAT CAN ADVERSELY AFFECT BONE MARROW FUNCTION?



Useless leukaemic cells filling up the bone marrow.



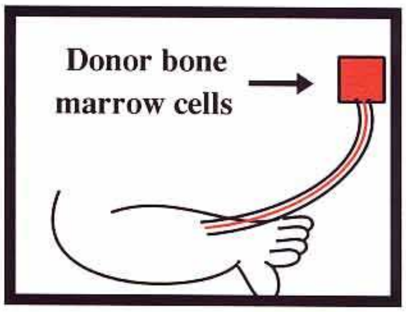
Inherited gene defects affecting cells in the marrow (see page 294).



Large doses of radiotherapy and cytotoxic drugs.

Jasper undergoes his chemotherapy.

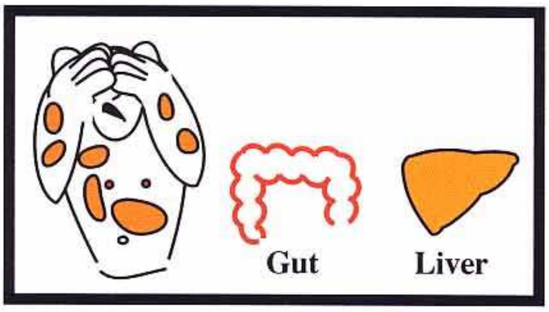
In the meantime, a donor was found and some of his bone marrow removed.



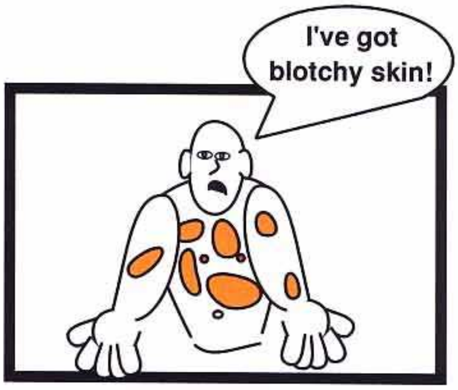
On entering one of Jasper's veins, the cells will find their own way to his bone marrow.

To prepare Jasper's body for a bone marrow transplant, his bone marrow is emptied of all resident cells. Then, when he is given the bone marrow cells, these will have space to move into and hopefully start to repopulate his bone marrow.

GRAFT - VERSUS - HOST DISEASE

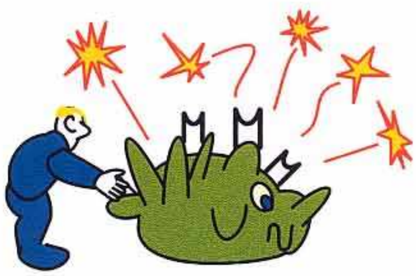


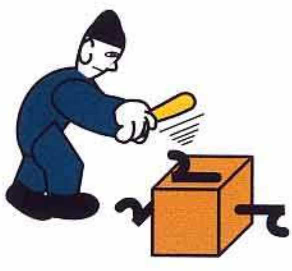
Jasper starts to experience serious side effects to his skin, gut and liver.



The infused cells have started to attack Jasper and could kill him.

This can occur when incompatible bone marrow cells are given to a host with few, if any, of their own immune cells.

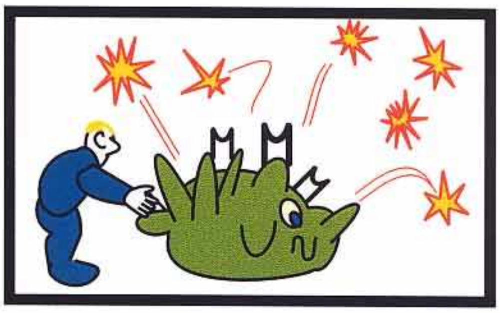




Mature T cells entering Jasper, perceive that they are encountering infected material, because their 'hands' fit his 'attack' and 'defence' proteins.

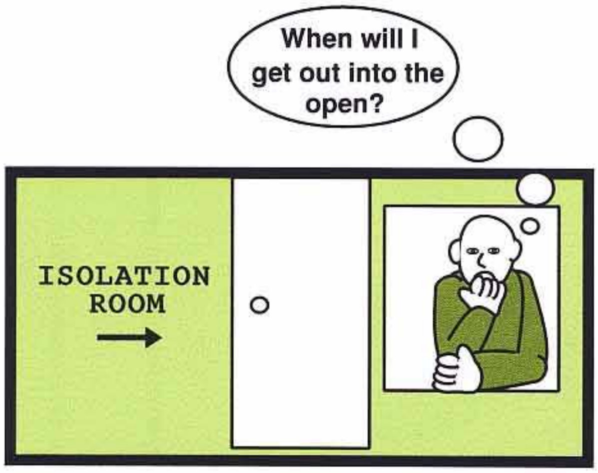
DANGER

Jasper must now undergo further chemotherapy, to quickly kill off the infused cells, before they kill him!



Ironically, part of the damage is due to the infused T cells, stimulating his resident macrophages.

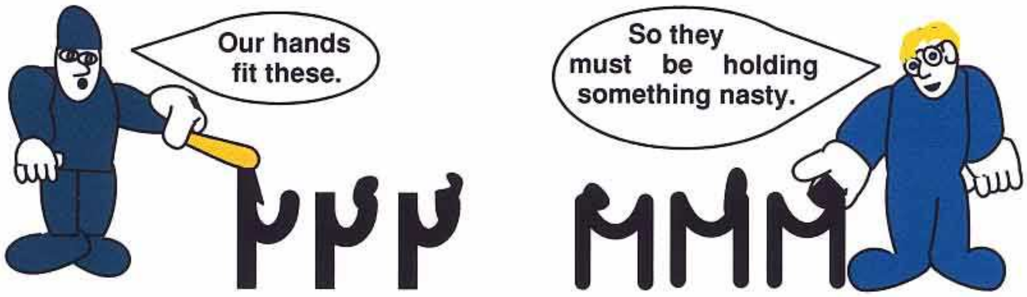
If the mature T cells are removed from the extracted bone marrow before it is given to the patient, then the risks of a graft-versus-host reaction occurring are minimised.



Sadly, a bone marrow transplant minus mature T cells, may now take much longer to repopulate a person's bone marrow.

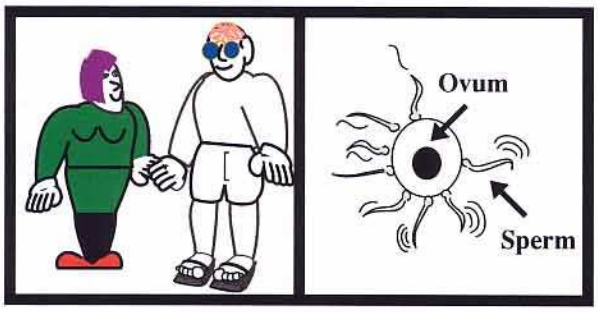
And while poor Jasper has only a few immune cells to protect him, he is at risk from life-threatening infections.

People with a severely depleted immune system may be referred to as 'immuno - compromised'.

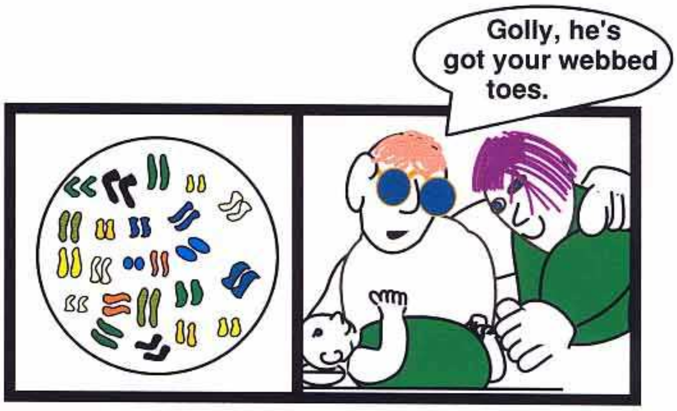


The problem, is that T cells in the extracted bone marrow, came from someone with different shaped 'attack' and 'defence' proteins. How we acquire these shapes, is now shown on the following pages.

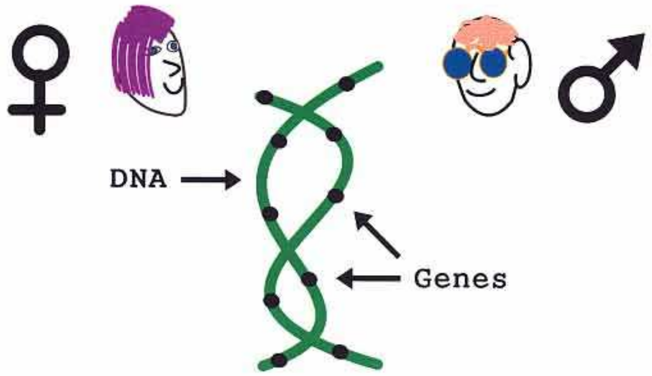
KERRY AND STEVE DECIDE TO MAKE A BABY



A sperm carrying 23 chromosomes, fertilises the mother's ovum, which also contains 23 chromosomes.

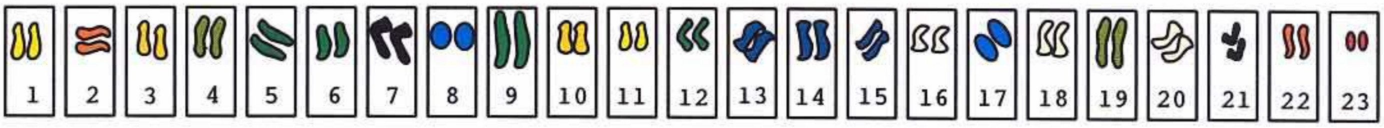


As the fertilised ovum now contains 23 pairs of chromosomes, the resulting baby will have characteristics (traits), from both parents.

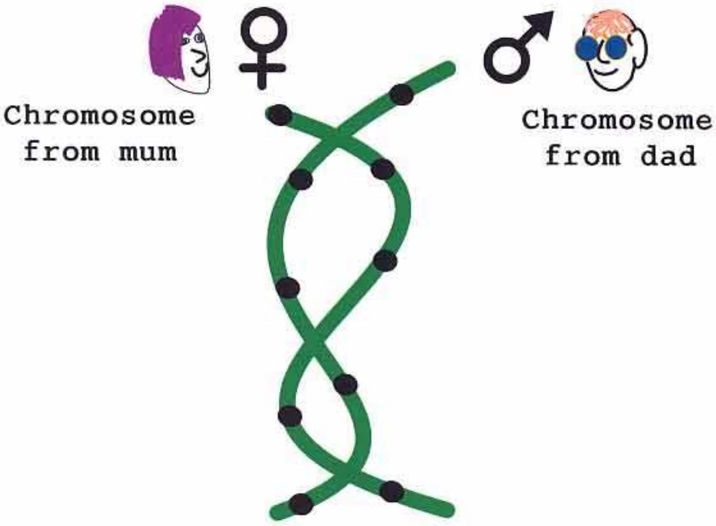


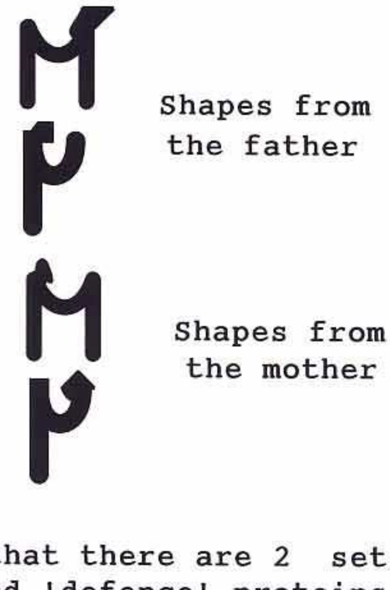
Each pair of chromosomes, has a strand of DNA from the mother and another strand of DNA from the father.

A CHILD GETS ITS GENES FROM BOTH PARENTS



In every nucleated cell in your body, are 23 pairs of chromosomes. Half of each pair comes from mum and the other half comes from dad.



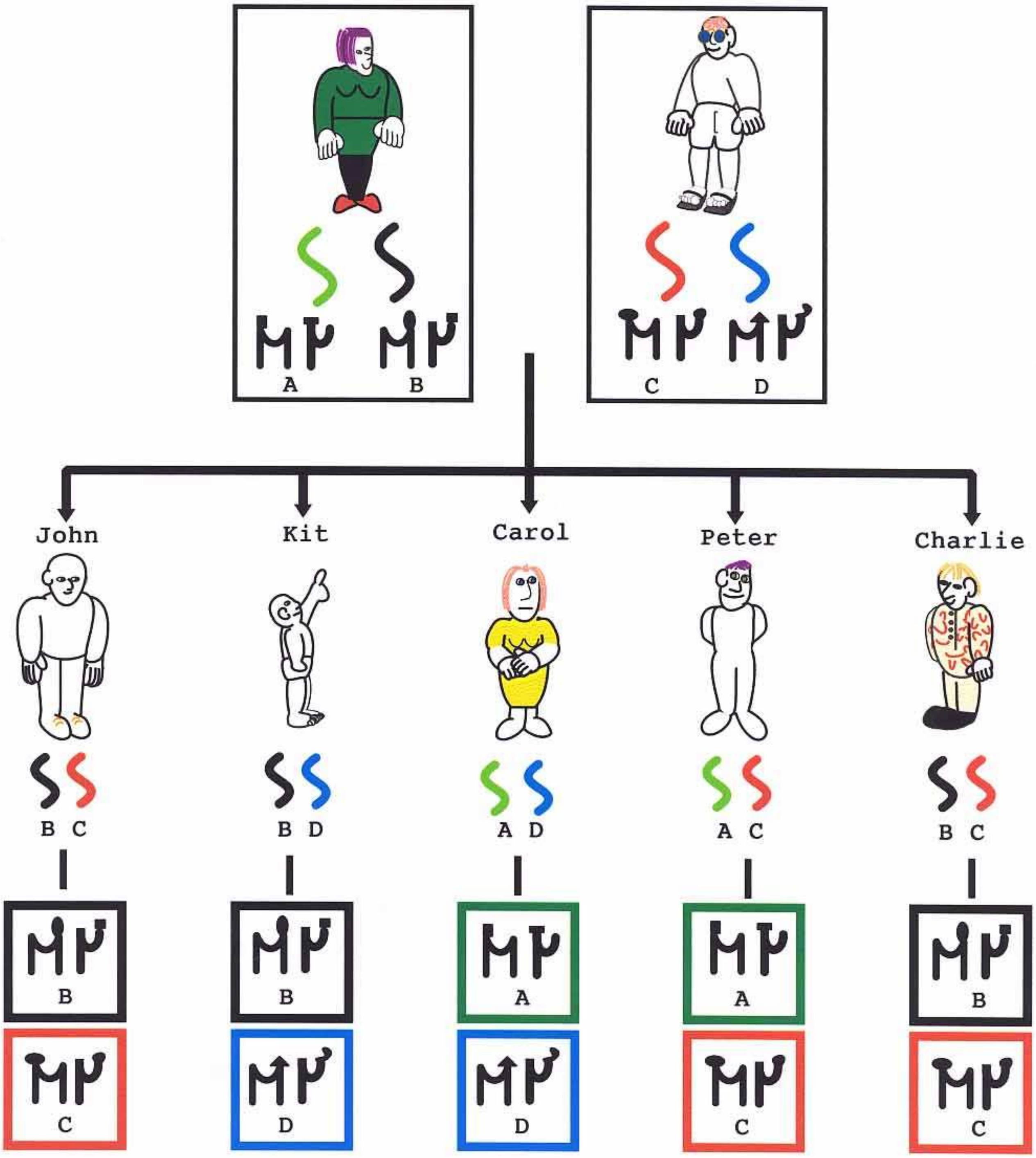


Along chromosome number 6, are the genes that code for the 'attack' and 'defence' proteins.

But note that there are 2 sets of 'attack' and 'defence' proteins. One set from dad and the other from mum.

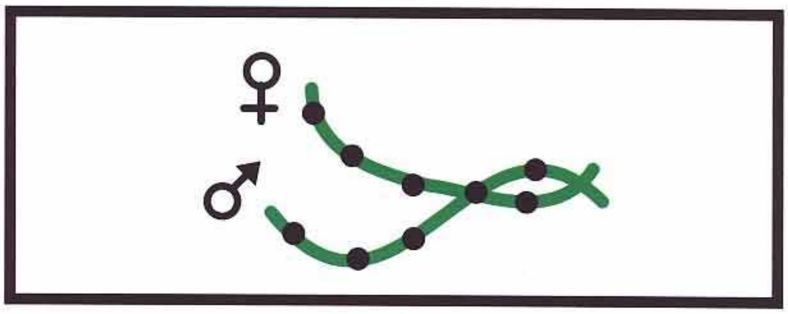
A child will get one strand of chromosome No.6 from one parent and the other strand of chromosome No.6 from its other parent.

Genes along chromosome No.6 code for both the 'attack' and 'defence' proteins.



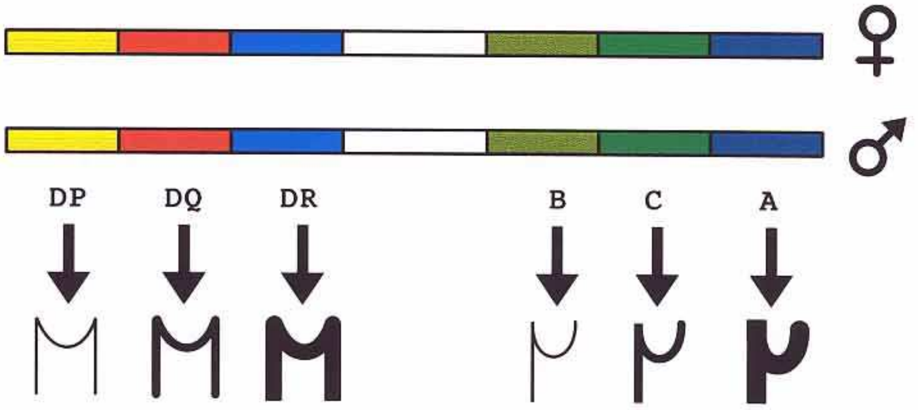
If Kerry and Steve have 5 children, it is possible that only 2 of their offspring will inherit the same gene combination and therefore the same shaped 'attack' and 'defence' proteins.

A CLOSER LOOK AT CHROMOSOME NUMBER 6



The string of genes along chromosome number 6 coding for the 'attack' and 'defence' proteins, are called the "major histocompatibility complex" (MHC) (see pages 77 and 110).

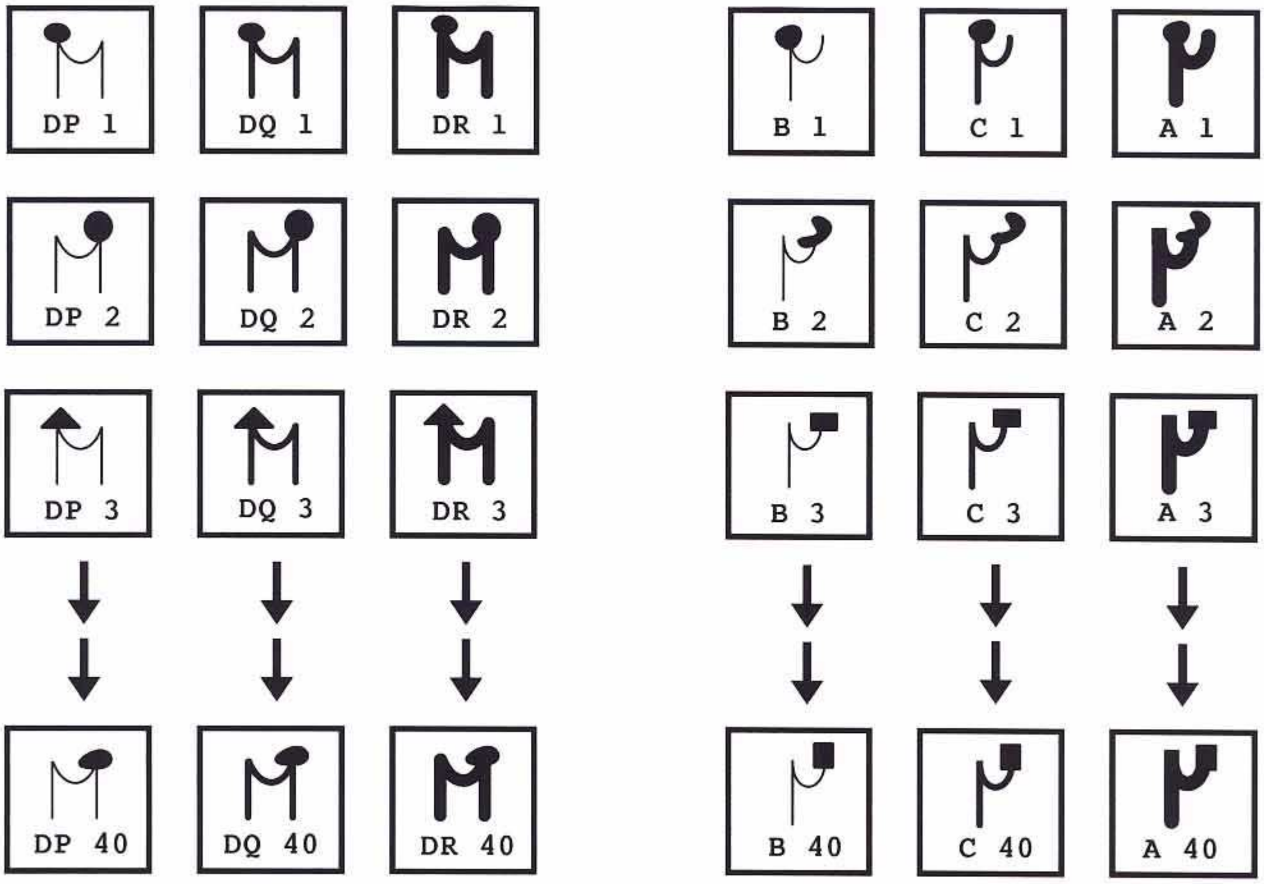
Here the genes making up the MHC have been enlarged.

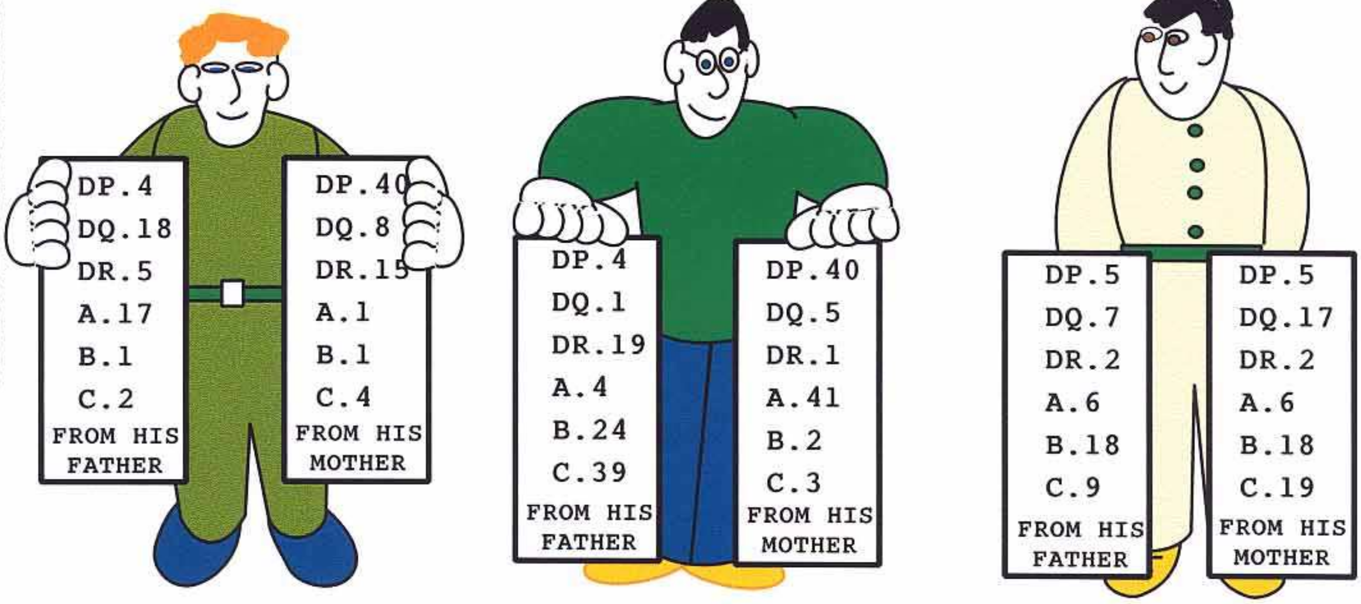


Everyone has 3 types of 'attack' proteins: DP, DQ and DR...
.... and 3 types of 'defence' proteins: A, B, and C....
...............inherited from each parent.

TISSUE TYPES

There are many different shaped 'attack' and 'defence' proteins and each of us inherits a certain set of shapes from our parents. It is this set of shapes, which constitutes someone's tissue type.





CHAPTER TWELVE

HYPERSENSITIVITY

Hypersensitive reactions occur, when the immune system injures the host, by reacting inappropriately or excessively.

Easy reading

Technical information

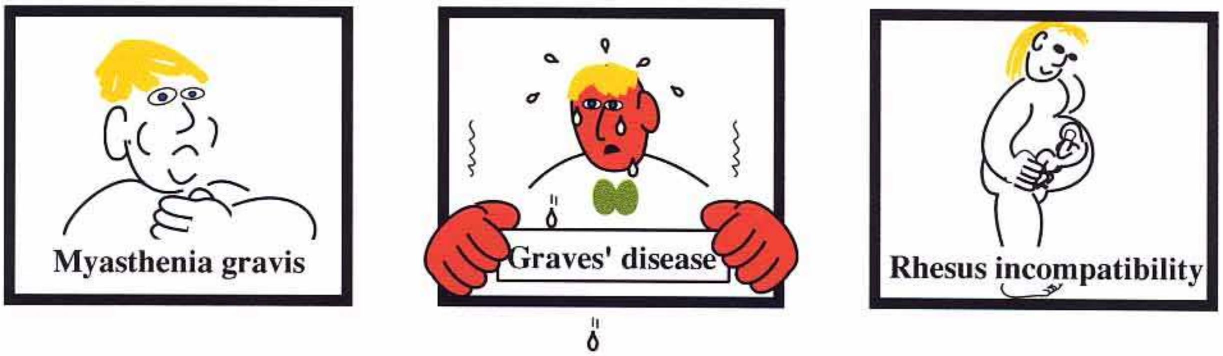
TYPE 1 HYPERSENSITIVITY

Type 1 hypersensitivity reactions can vary from a simple bout of sneezing, to a life-threatening anaphylactic reaction. However, what they have in common, is that the reactions occur within minutes of the person coming into contact with something (ie a peanut).

WHY ARE TYPE 1 HYPERSENSITIVE REACTIONS SO RAPID?

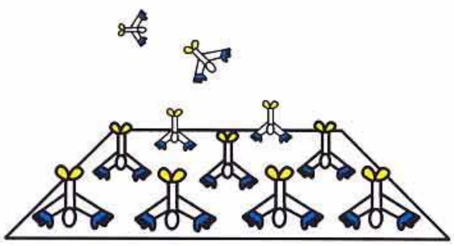
Adjoining IgE already lining surface of the mast cell, 'grab' the same object. This triggers the mast cell into releasing its stored histamine (see page 54).

TYPE 2 HYPERSENSITIVITY

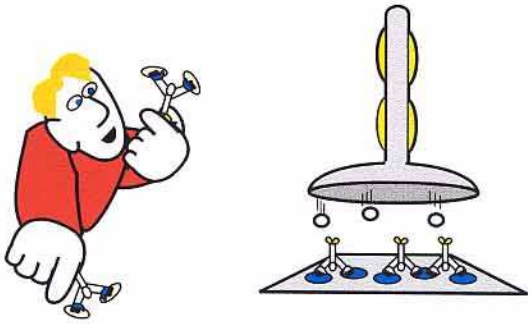


These are just a few examples of type 2 hypersensitive reactions.

THE MECHANICS OF A TYPE 2 HYPERSENSITIVE REACTION



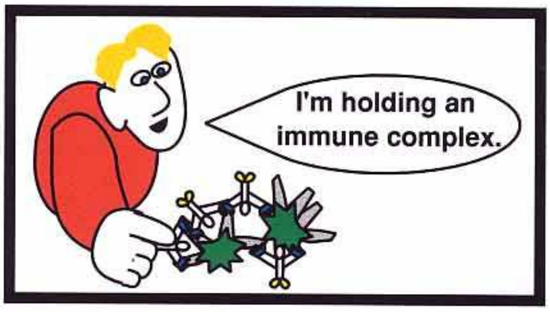
IgG antibodies attach onto the surface of a cell, one layer deep.



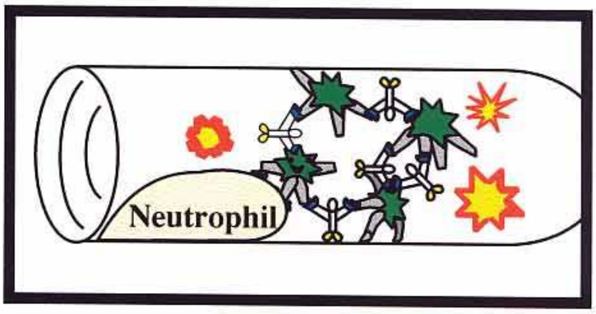
The affected cell is then 'eaten', 'blown apart' by complement, or simply prevented from working.

TYPE 3 HYPERSENSITIVITY

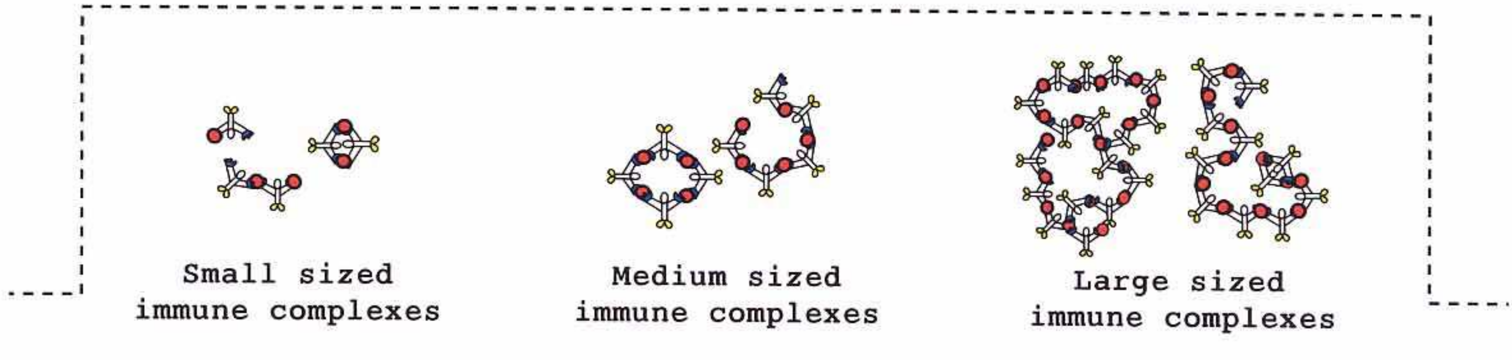
Type 3 hypersensitive reactions produce characteristic lumpy - bumpy deposits.



Normally, material clumped together by antibodies (an immune complex), is 'eaten' by macrophages living in the spleen or the liver.



But if an immune complex gets trapped in a blood vessel, an inflammatory response will quickly follow.

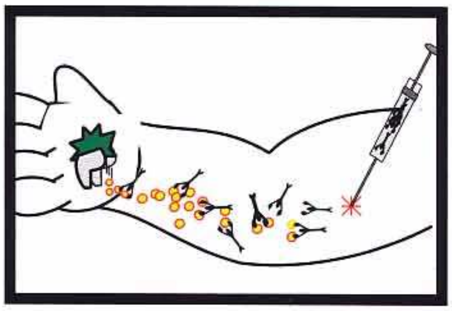


Most people make small or large sized complexes, which are eliminated in the liver and spleen. But a few people produce medium sized complexes, which for an unknown reason, tend to become trapped in the wrong places!

SERUM SICKNESS

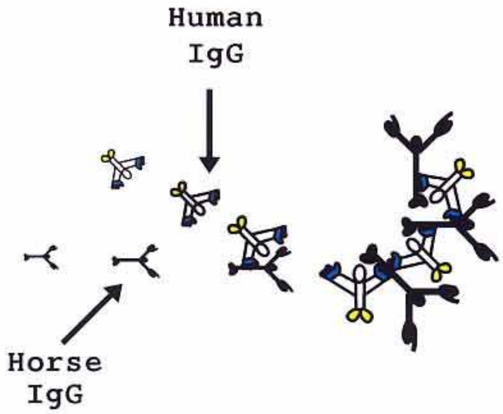
This is an example of a systemic type 3 hypersensitive reaction, where immune complexes become deposited all over the body.

During the First World War, many injured soldiers died from tetanus (see page 106).

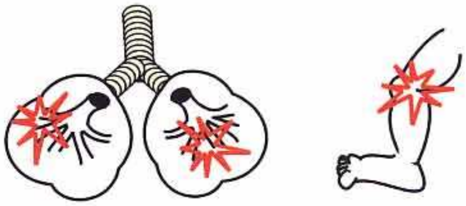


To prevent this, injured soldiers were given horse serum, containing anti-tetanus IgG antibodies.

But a few of the soldiers then experienced kidney problems, skin rashes and joint pains.



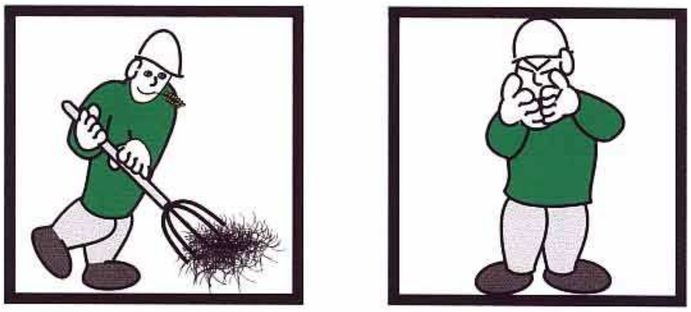
As horse IgG is foreign material, human IgG were made against them. The resulting complexes, would then be eliminated in the spleen.



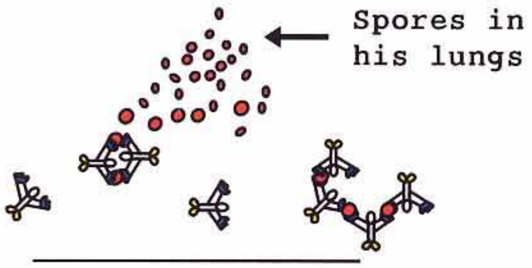
But for a few, these complexes became lodged in the kidneys, lungs or joint synovium, which caused an inflammatory response.

FARMER'S LUNG

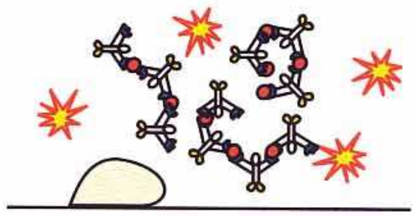
An example of a local type 3 hypersensitive reaction.



8 to 10 hours after working with spoilt hay, this farmer experiences breathing problems.



Spores entering his lungs are 'grabbed' by IgG antibodies.

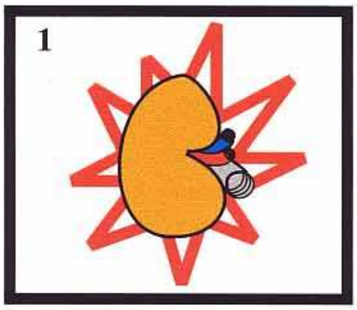


Complement activation attracts neutrophils and these increase the inflammatory response.

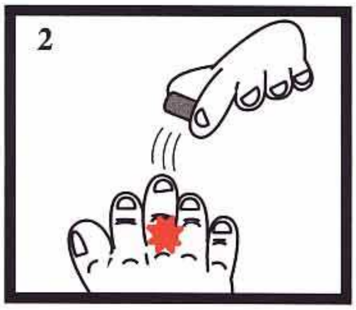
When immune complexes accumulate in the tissues during a local type 3 reaction, it is sometimes called an "Arthus reaction".

TYPE 4 HYPERSENSITIVITY

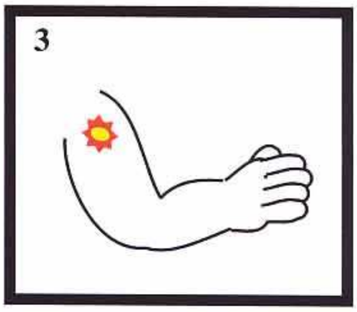
Examples of this type of hypersensitivity include:-



Transplant rejection.



Contact sensitivity.



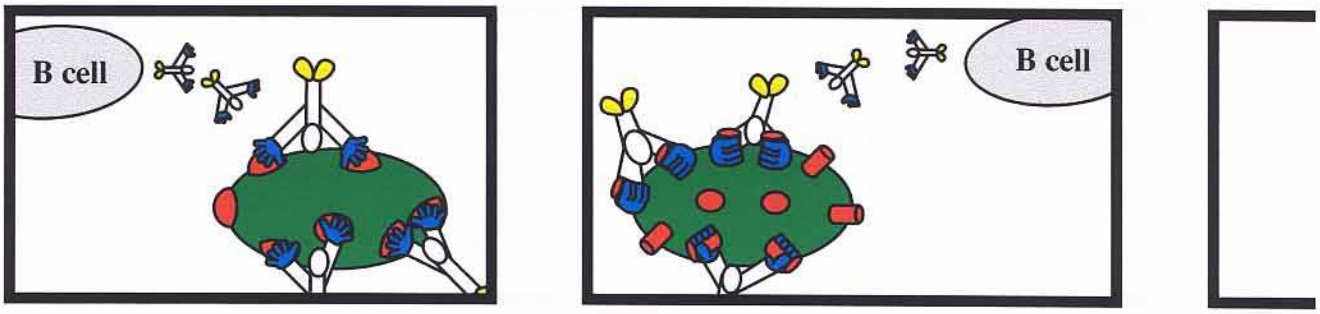
A positive heaf test.

A skin rash can develop a day or so after coming into contact with certain chemicals or metals (ie a nickel ring).

Type 4 hypersensitivity reactions result from the over-stimulation of local macrophages by T helper cells.

CHAPTER THIRTEEN

THE EXTENDED ROLE OF ANTIBODIES

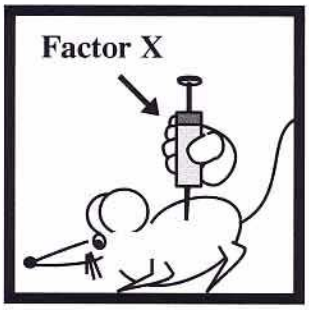


Antibodies will have the same shaped 'hands' as the B cell which released them, as shown on page 63.

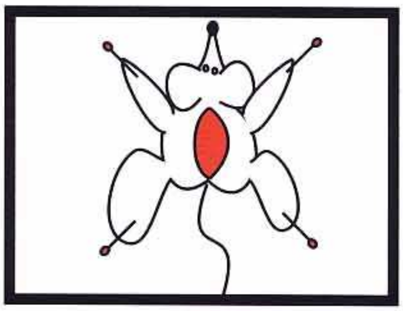
Easy reading

Technical information

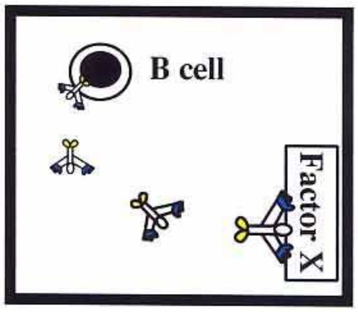
But how do you find a B cell that produces antibodies, which have a 'hand' shape that fits what you want?



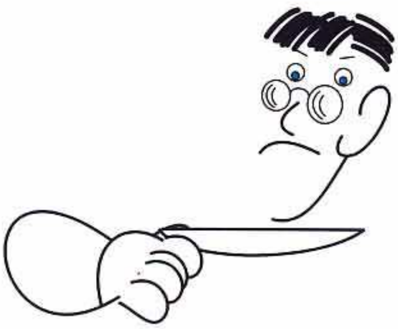
A mouse is injected with factor X.



2 weeks later it is killed and organs containing B cells like the spleen, are removed.

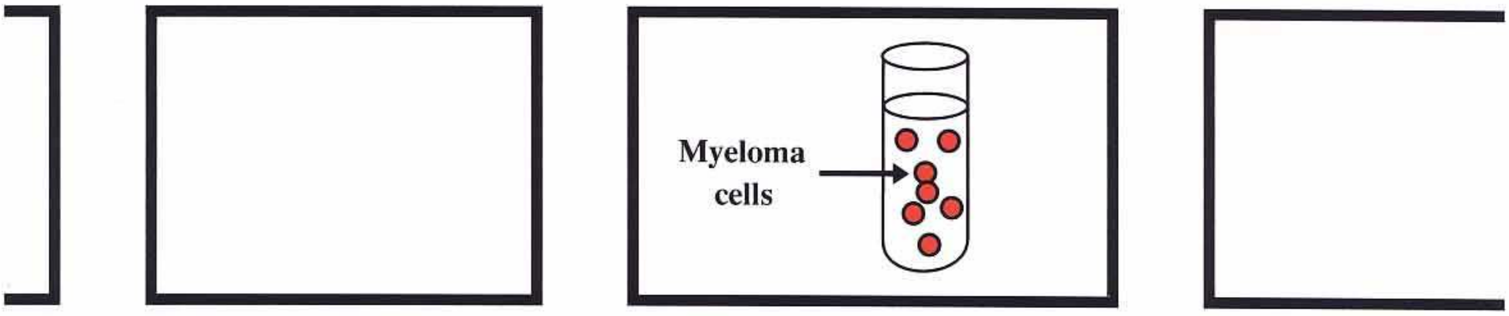


This mouse B cell, is releasing antibodies with 'hands' that 'fit' factor X.

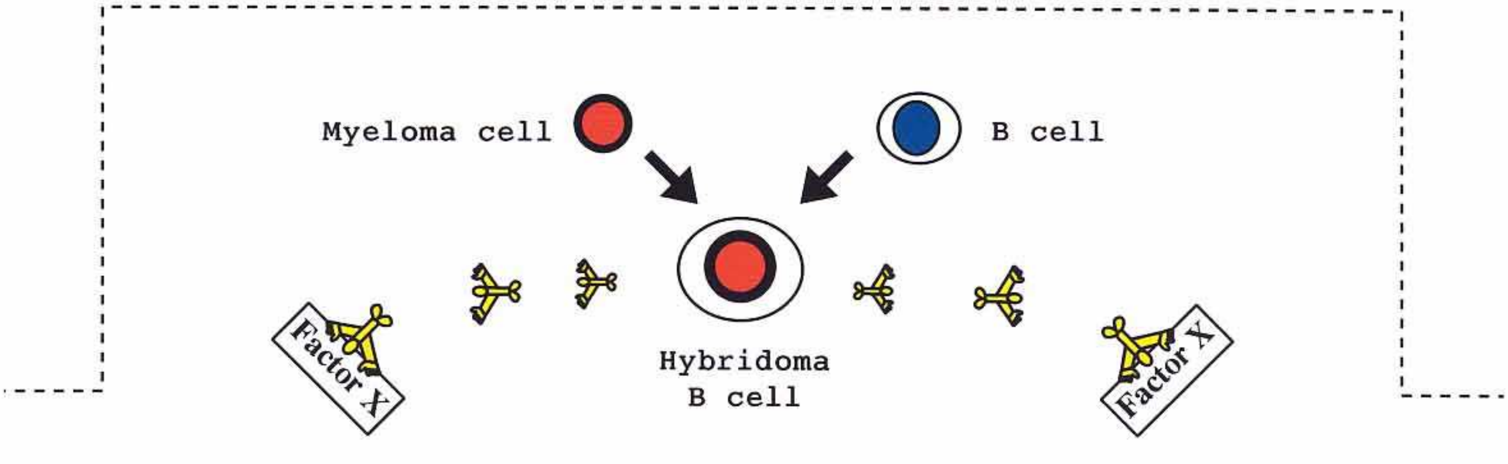


```
Unfortunately, when kept in an artifical
environment, B cells like all normal
cells will die after only a few days.
```

HYBRIDOMA B CELLS

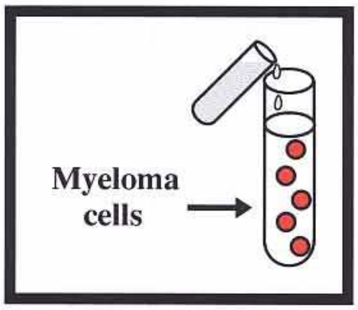


But cancer cells, like these myeloma cells, are able to survive indefinitely in an artificial medium.

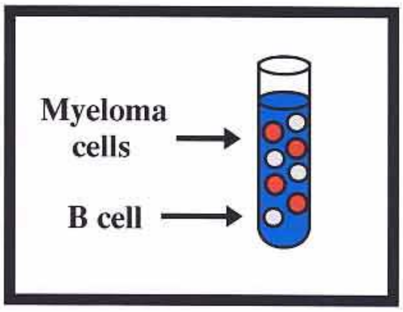


So by fusing a myeloma and B cell together, you end up with a hybridoma B cell. This cell will live indefinitely and make antibodies with 'hands' that fit a known substance.

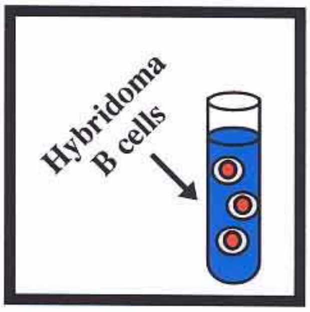
HOW TO FORCE THE MYELOMA AND B CELL TO FUSE



First the myeloma cells have their TK & HGPRT enzymes destroyed.



The treated myeloma cells are then placed in a HAT solution, along with B cells.



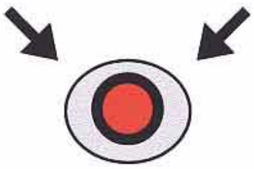
A couple of weeks later, only hybridoma B cells are left.

HGPRT : Hypoxanthine - guanine phosphoribosyl transferase
TK : Thymidine kinase
HAT : Hypoxanthine, aminopterin and thymidine

WHY DO THESE 2 CELLS FUSE TOGETHER?

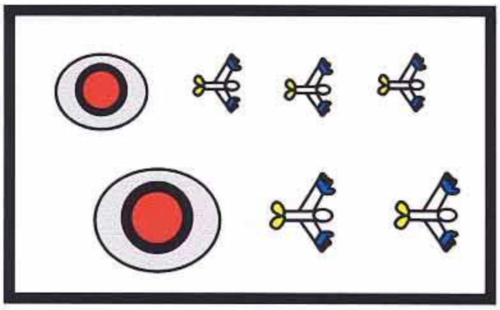
A myeloma cell needs the TK and HGPRT enzymes from the B cell to survive.

The B cell needs the immortality of the myeloma cell to survive.

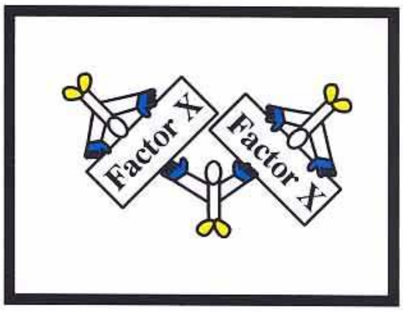


Hybridoma B cell

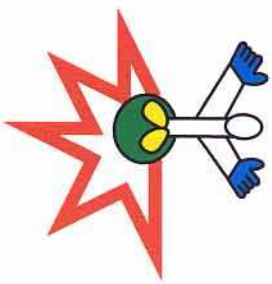
MONOCLONAL ANTIBODIES



Clones from the original hybridoma B cell, will all release antibodies with 'hands' that 'fit' the same thing.

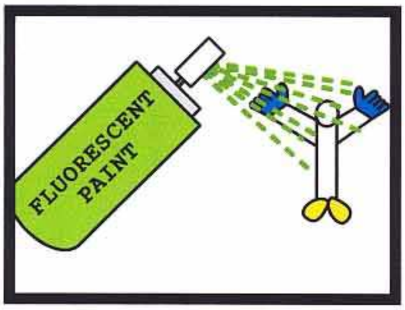


Hence, the antibodies from a hybridoma B cell are called "monoclonal antibodies".

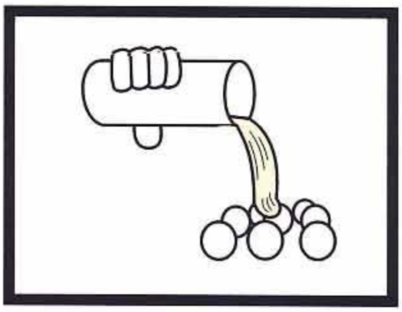


Fluorescent, radioactive or enzyme materials, can all be attached to the 'body' of an antibody and have no effect on their 'hands'.

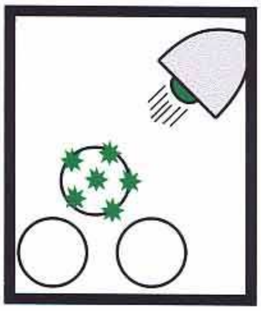
LABELLING



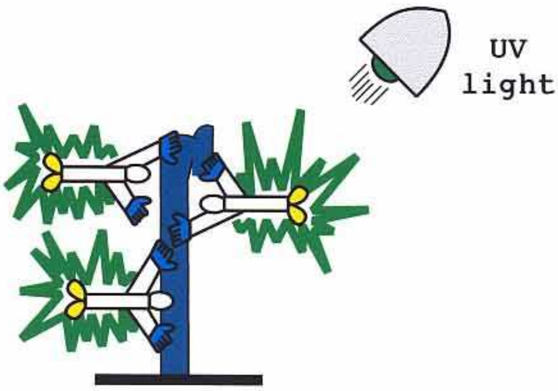
Some monoclonal antibodies, with 'hands' that fit the CD4 molecule, are labelled with fluorescent material.



Fluid containing the labelled IgG, is then applied to these cells to see if any of them are T helper lymphocytes.

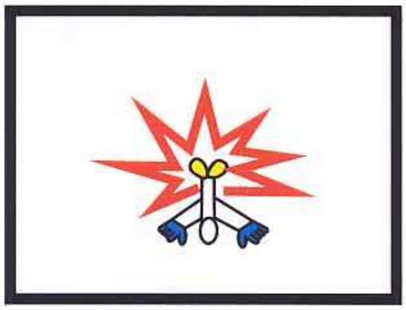


One of the cells now glows under ultraviolet light.



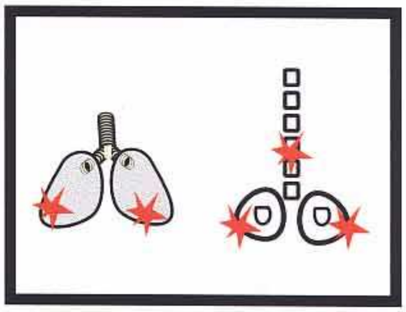
Here a CD4 molecule has been enlarged to show the labelled IgG.

MAGIC BULLET OR RUSSIAN ROULETTE?



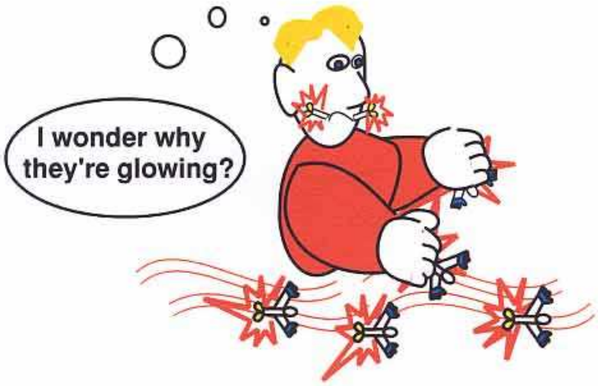
Monoclonal antibodies with 'hands'that 'fit' a particular cancer, have a radioactive isotope attached.

These are then given to the patient.

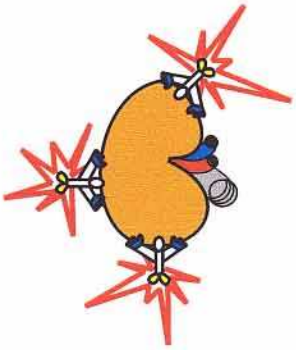


Hopefully they will attach onto the tumour and any secondaries and kill them.

HOWEVER!!!



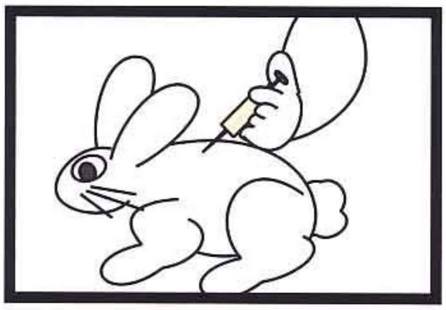
The labelled antibodies could kill resident macrophages, who may 'eat' them as they are foreign material.



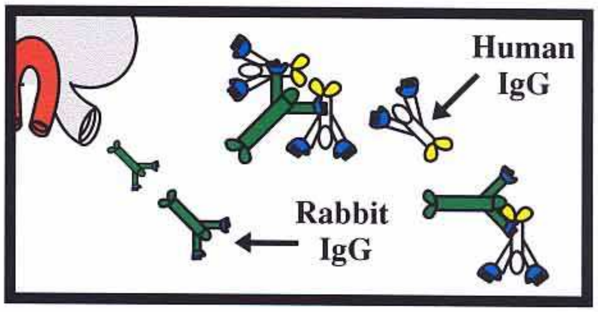
And if their 'hands' happen to fit any normal cells, then these too might be killed.

THE COOMBS' TEST

This test which has many applications, uses antibodies made inside an animal which have 'hands' that 'fit' human antibodies.

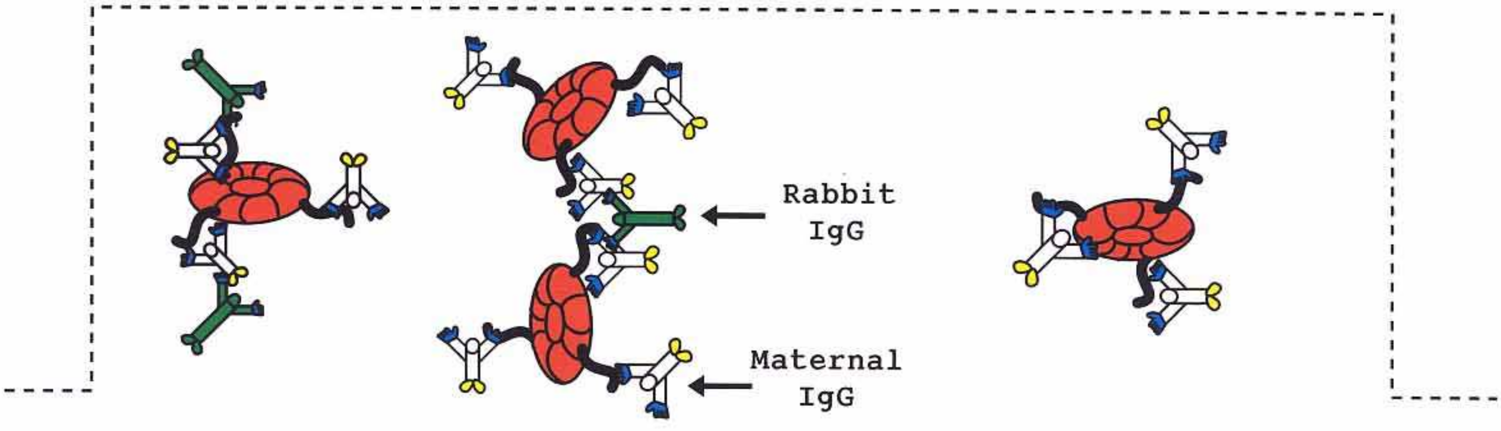


Human antibodies are injected into an animal such as a rabbit.



A couple of weeks later and the rabbit's immune system starts making antibodies, to eliminate the human antibodies.

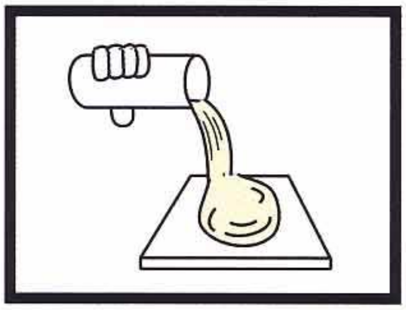
These anti-human antibodies are now extracted from the animal.



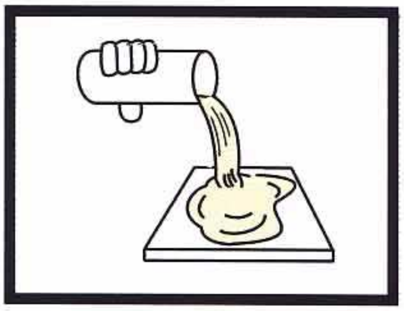
If blood from a 'blue baby' (see page 172) clumps when a Coombs' test is conducted, it shows that the problem is due to the mother making anti-rhesus antibodies.

ONE OF THE TESTS FOR AIDS

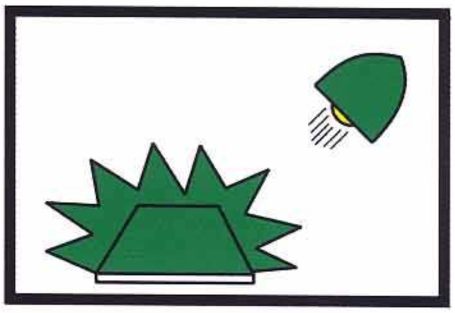
A couple of weeks after becoming infected by this virus, anti-AIDS antibodies will start to appear in the patient's blood.



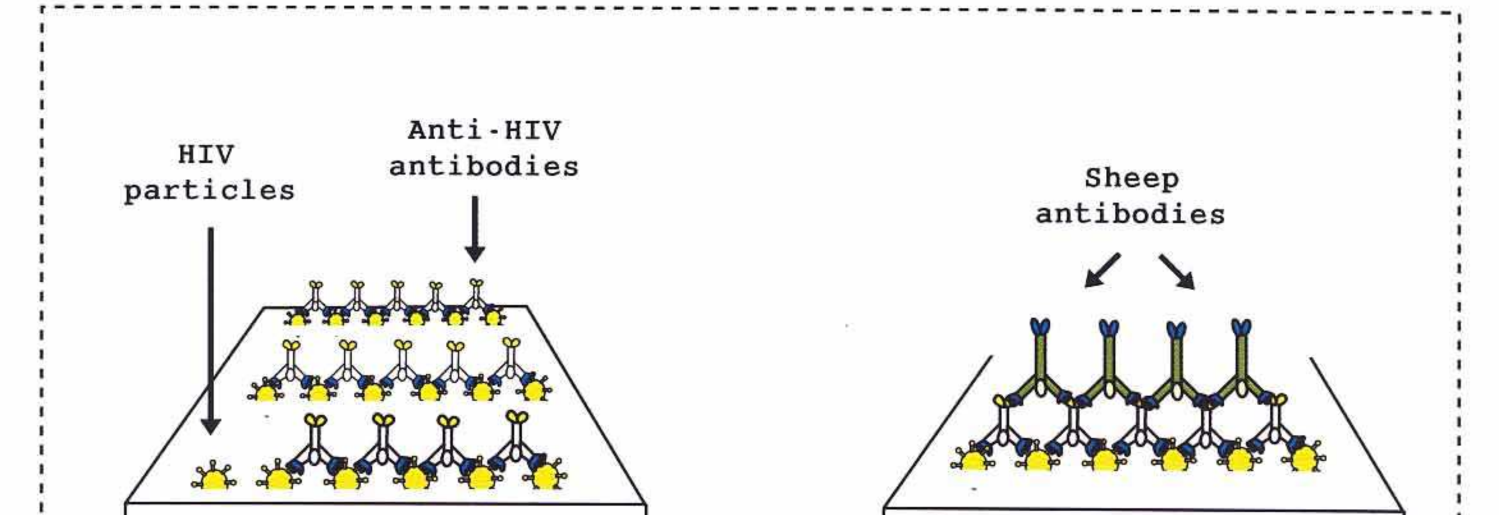
Serum from the patient is applied to a gel impregnated with the AIDS virus.



Fluorescent labelled anti-human antibodies, are then applied to the gel.



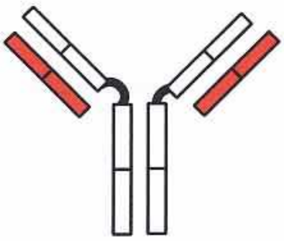
If the gel now fluoresces under ultraviolet light, the patient is infected with the AIDS virus.



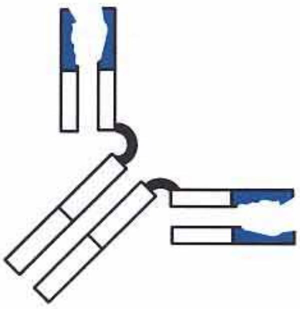
A person infected with the AIDS virus, will have antibodies in their blood, which will attach onto the HIV particles in the gel.

Note how the fluorescent labelled sheep antibodies, can now attach onto the anti-HIV antibodies.

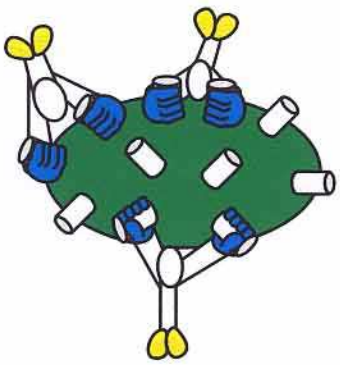
A BIT OF JARGON



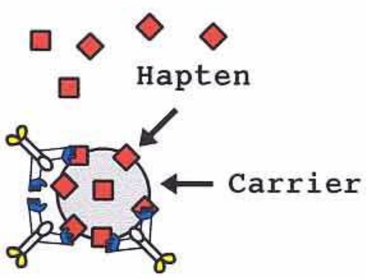
Although there are actually 2 types of antibody light chain called "kappa" and "lambda", a B cell is only able to make one or the other, never both.



A paratope is the technical name given to the part of the antibody's 'hand', that fits around something.



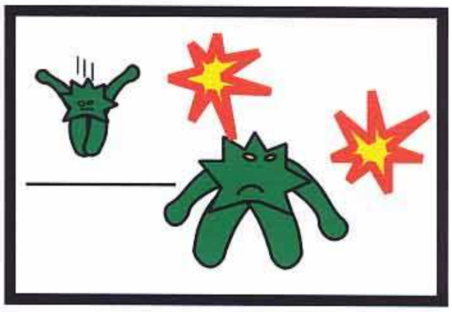
An epitope is the part (shape) that the antibody's 'hand' fits around.



A hapten is a particle which is too small to elicit an antibody response, until it is attached onto a larger carrier molecule.

CHAPTER FOURTEEN

COMPLEMENT



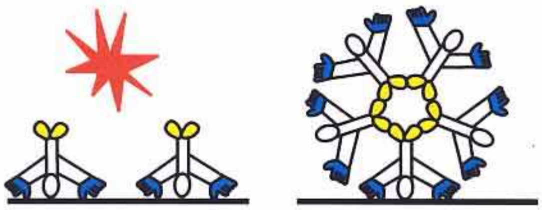
A burglar alarm will warn the occupants of a break in.

Likewise, when complement is activated, it warns the immune system of invading microbes.

Easy reading

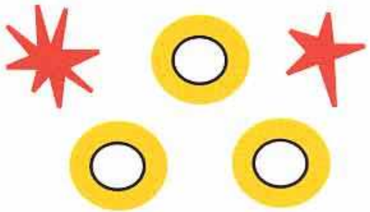
Technical information

HOW COMPLEMENT IS ACTIVATED



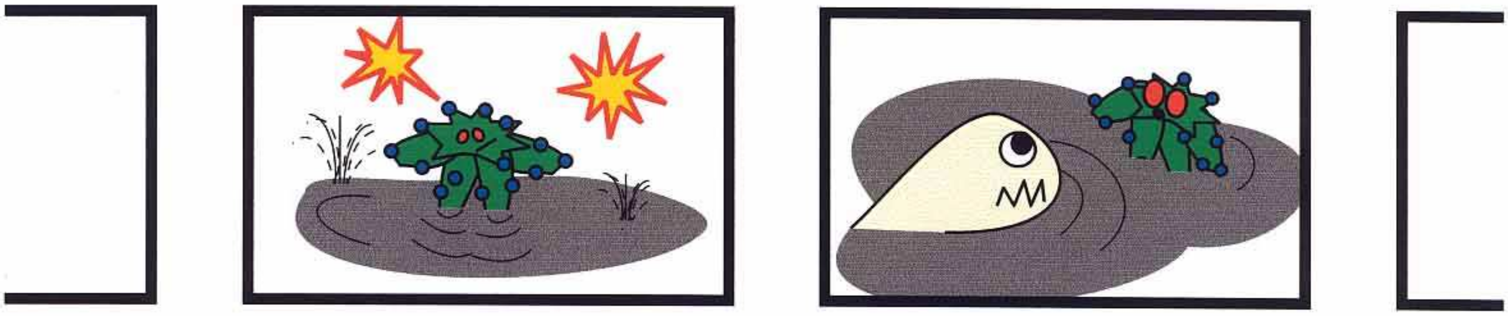
THE CLASSICAL PATHWAY

This involves IgG or IgM antibodies attaching onto something (see page 270).



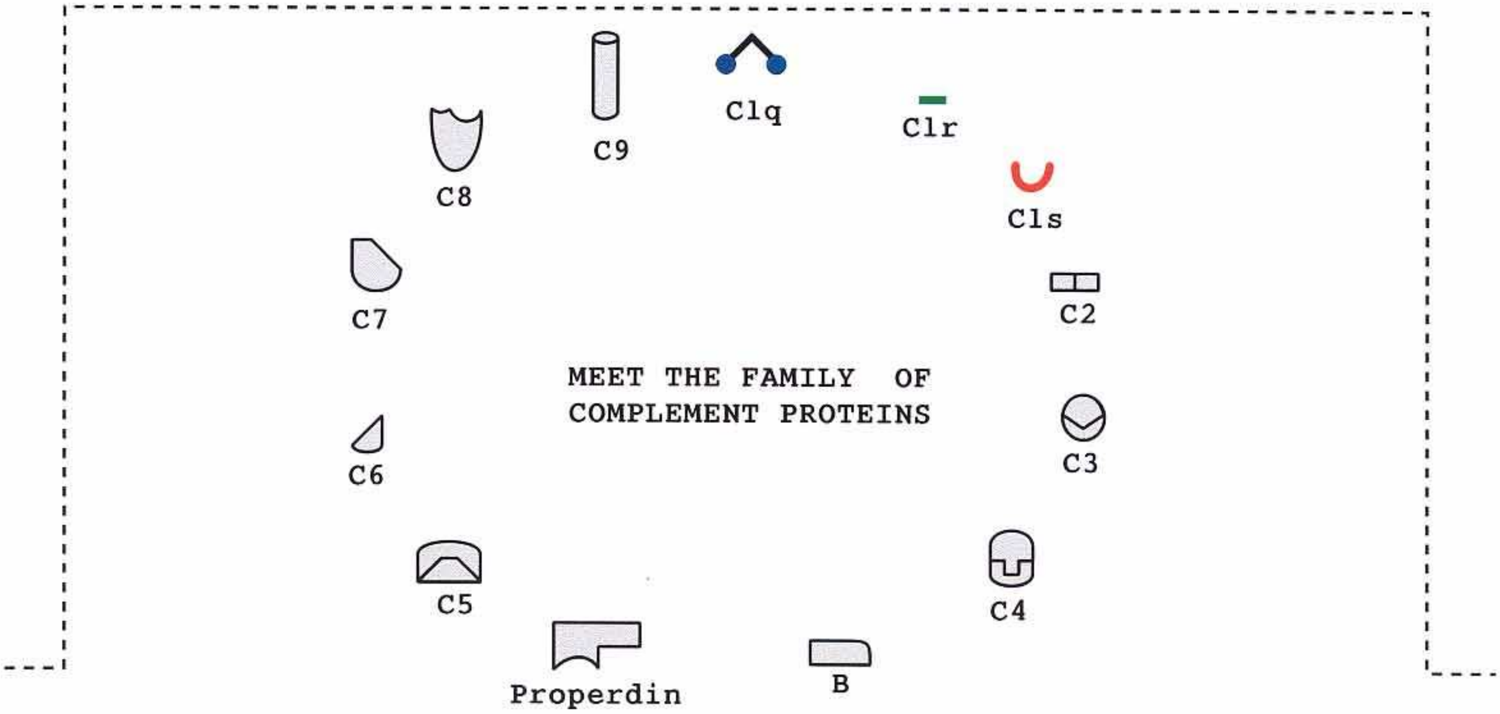
THE ALTERNATIVE PATHWAY

This occurs if complement comes into contact with certain foreign substances (see page 271).



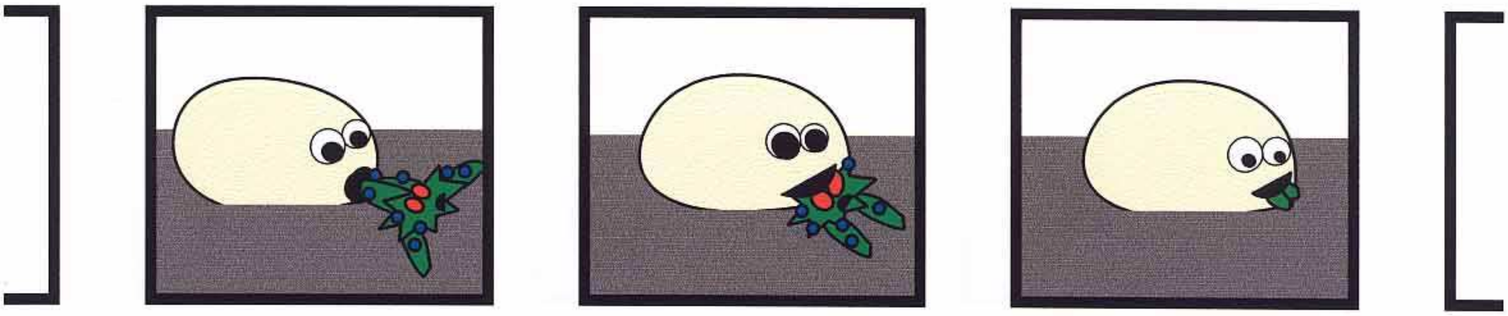
Complement is quickly activated and coats the microbe.

Then, like a creature from the deep, a neutrophil emerges.

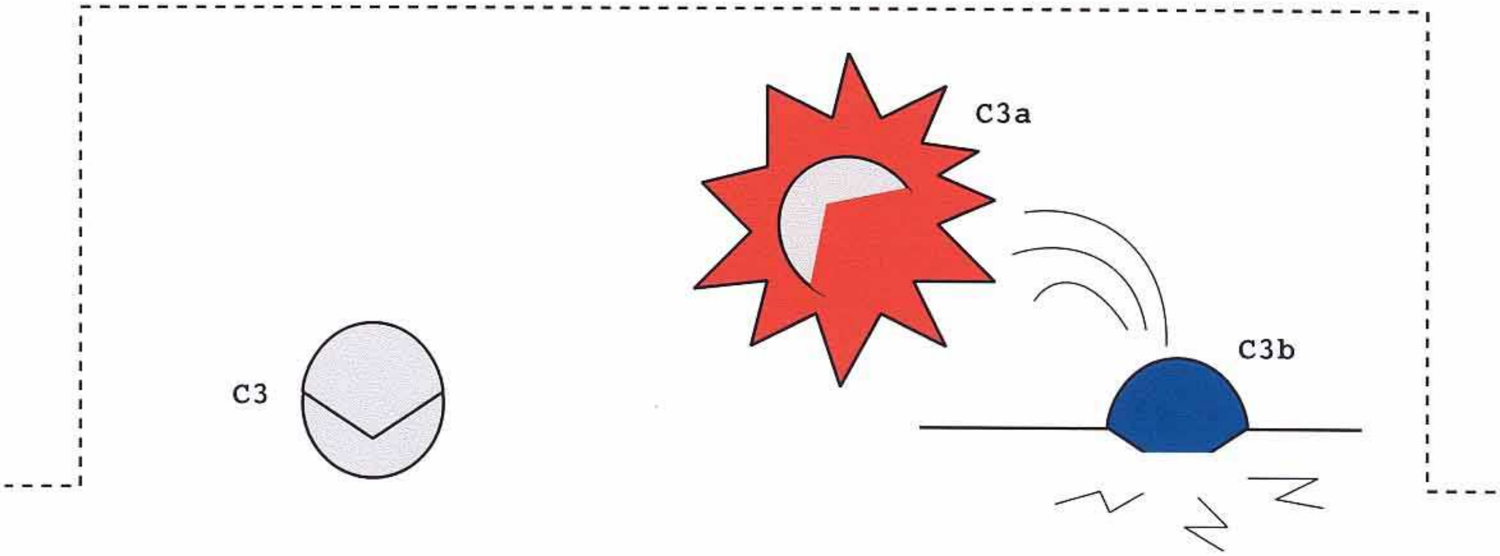


As complement is not one protein but many, they are sometimes referred to as the complement family. Found in blood in their inactive form, complement proteins are permanently damaged if heated above 56°C.

THE MICROBE IS QUICKLY GOBBLED UP



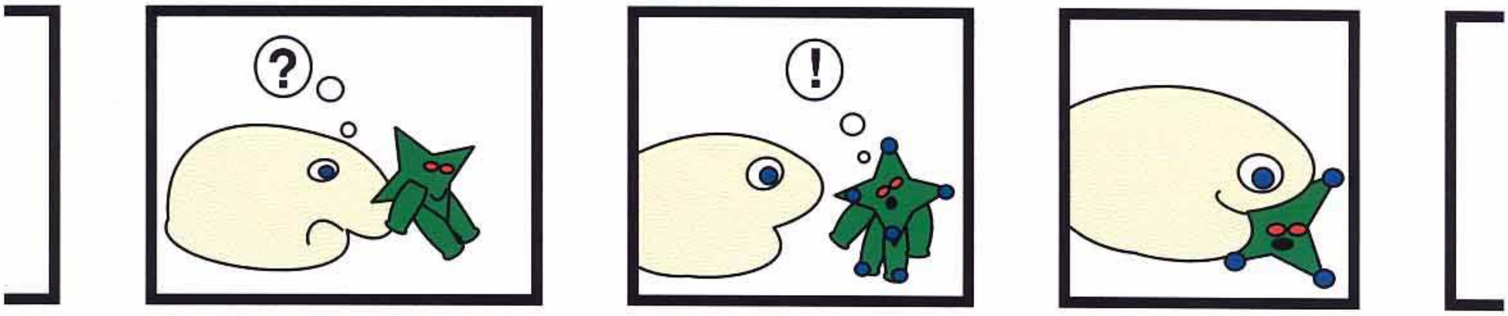
'Eating' this microbe is especially easy, as it is coated in complement C3b.



When complement C3 is activated, certain internal bonds are broken and it splits in 2.

C3a releases inflammation and C3b binds to the surface of whatever triggered the reaction.

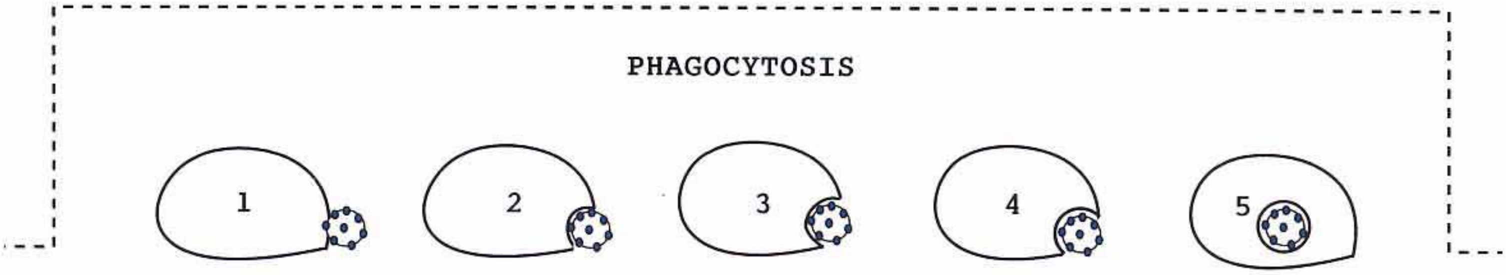
WHY IS IT EASIER TO 'EAT' THINGS COATED IN C3b?



Some bacteria have a 'slimy' exterior, which stops them from being 'eaten' easily.

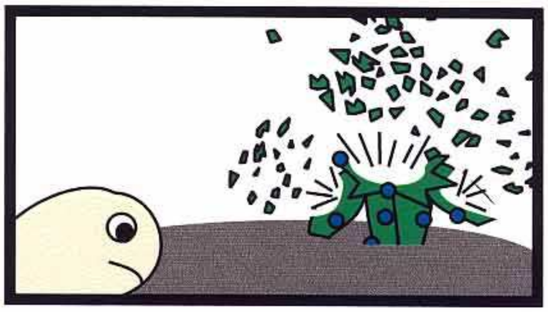
But usually it is not long before they are coated in complement C3b.

Now the immune cell can quickly 'gobble' up the bacteria.

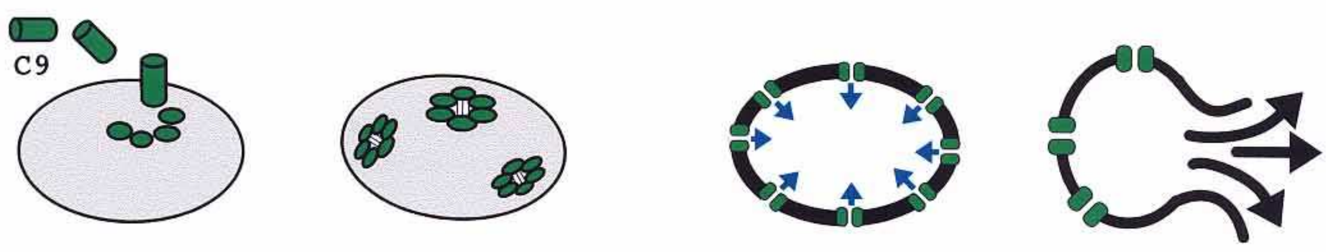


Macrophages and neutrophils have C3b surface receptors which 'lock' onto the C3b's that coat a microbe. This allows their membrane to envelop the microbe, like a zip being fastened.

THIS NEUTROPHIL ARRIVES TOO LATE!!!



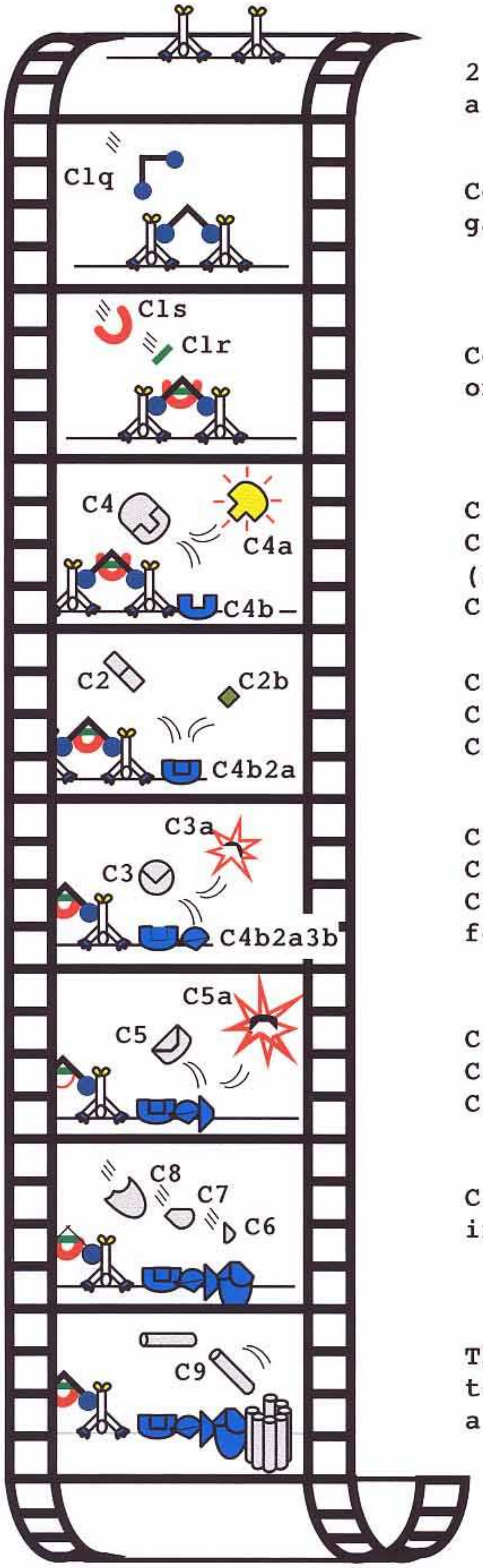
Just as he arrives, the microbe explodes.



Complement C9 pierces the microbe's membrane, forming round structures called "membrane attack complexes".

These allow fluid to flow into the microbe, causing it to swell and then burst.

THE CLASSICAL PATHWAY FOR COMPLEMENT ACTIVATION



2 IgG must first attach onto a surface, very close together.

Complement C1q can now bridge the gap between the 2 IgG antibodies.

Complement C1r and C1s then attach onto the underneath of C1q.

C1s can now cleave complement C4.
C4a goes off with a small 'bang' (see page 277).
C4b fixes onto the membrane.

C2 is now cleaved.
C2a joins C4b to form C3 convertase (C4b2a).
C2b diffuses away.

C3 convertase cleaves another C3 protein.
C3a goes off with a 'bang' (see page 277).
C3b attaches to C3 convertase to form C5 convertase (C4b2a3b).

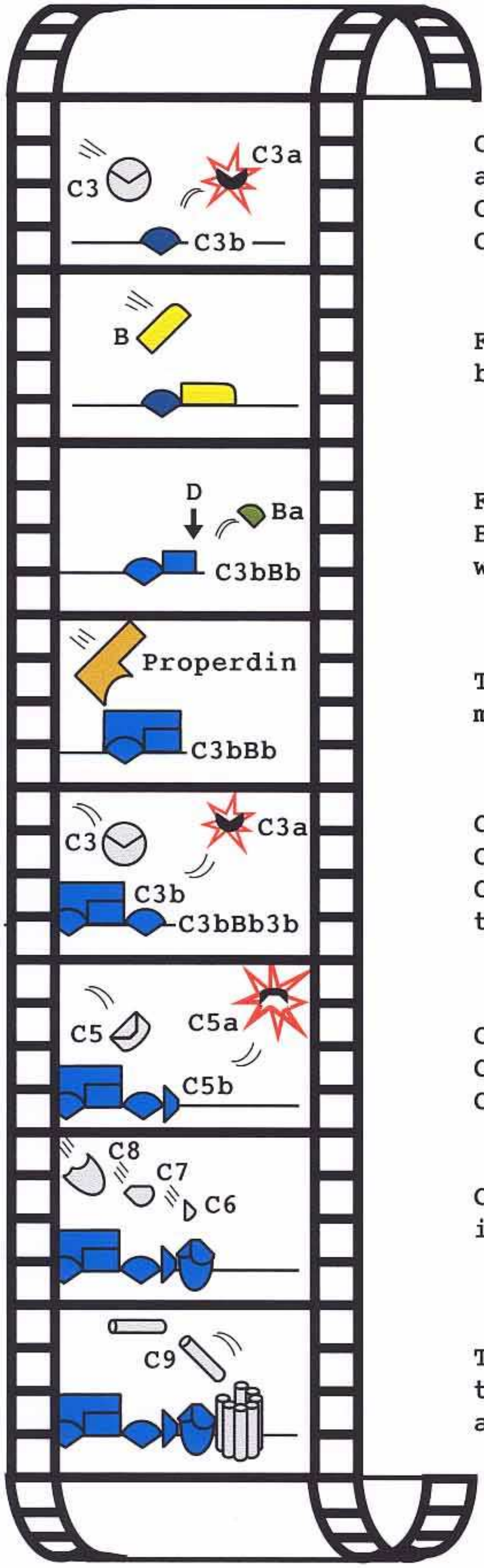
"THE FINAL COMMON PATHWAY"

C5 convertase cleaves C5.
C5a goes off with a large 'bang'.
C5b binds to the C5 complex.

C6, C7 AND C8 now insert into the microbe's membrane.

This heralds the insertion of up to 15 C9's, which polymerise into a membrane attack complex (MAC).

THE ALTERNATIVE PATHWAY FOR COMPLEMENT ACTIVATION



Complement C3 comes into contact with a microbe's surface and splits in 2.
C3a goes off with a 'bang'.
C3b attaches to the microbe's surface.

Factor B now combines with C3b, but by attaching it becomes unstable.

Factor D cleaves factor B.
Ba diffuses away, leaving Bd attached, which forms C3 convertase (C3bBb).

The complement protein properdin must now stabalise C3 convertase.

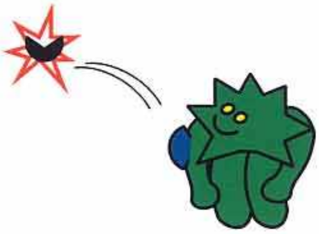
C3 convertase cleaves another C3.
C3a goes off with a 'bang'.
C3b attaches onto C3 convertase to form C5 convertase (C3bBb3b).

"THE FINAL COMMON PATHWAY"

C5 convertase cleaves C5.
C5a goes off with a large 'bang'.
C5b binds to the C5 complex.

C6, C7 AND C8 now insert into the microbe's membrane.

This heralds the insertion of up to 15 C9's, which polymerise into a membrane attack complex (MAC).



The alternative pathway is triggered when complement comes into contact with:- plasmin, lipopolysaccharide, toxin molecules, yeast cell walls and thromboxane-A2.

Complement activation leads to an expanding sequence of events, so that an object is rapidly coated in many C3b's. It is an example of a positive feedback reaction.

SAFETY

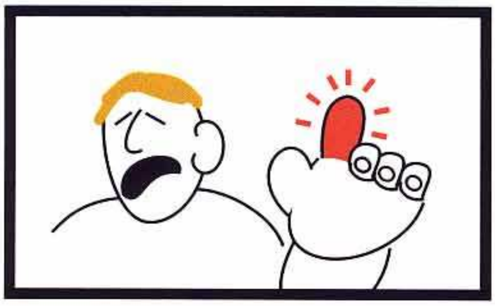
To prevent complement being accidentally triggered, the insides of our bodies are lined in 'factors', to stop this happening.

CHAPTER FIFTEEN

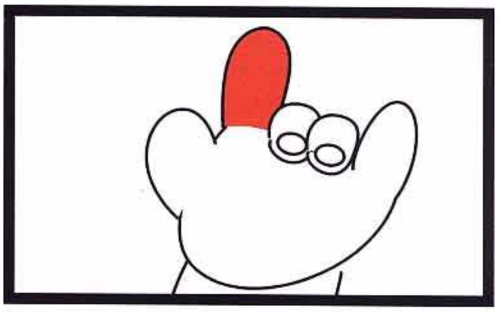
INFLAMMATION

IT'S A PAIN!!

But inflammation is one of the body's first lines of defence against infection.



The classic signs of an inflammatory response are:- heat, pain, redness, swelling and a loss of function.

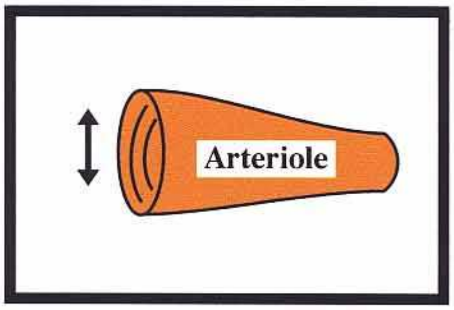


The redness, heat and swelling are due to an increased blood flow now entering the affected area.

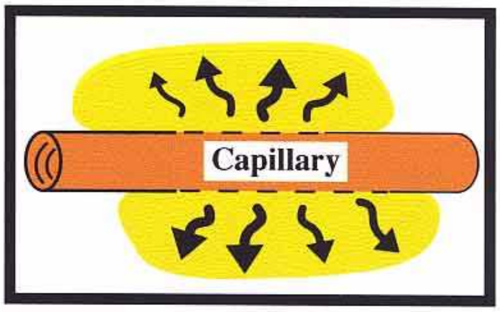
Easy reading

Technical information

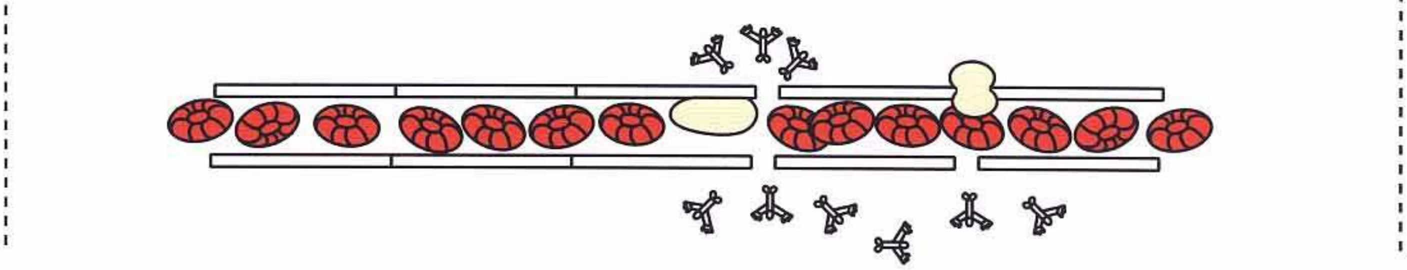
The increased blood supply diverts larger numbers of immune cells, antibodies etc., into the affected area.



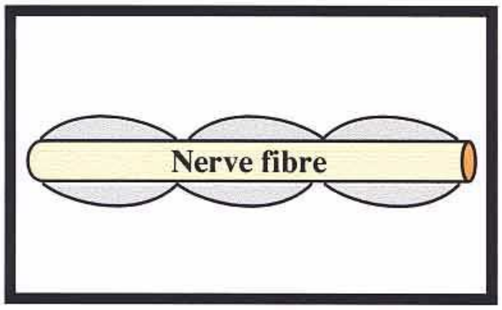
Arterioles supplying the affected part of the body dilate, allowing more blood to enter the area.

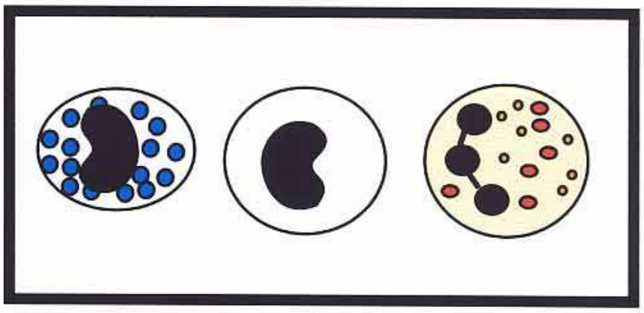


Gaps in the capillary walls in the affected area also widen, to allow more fluid to leak into the tissues.



The wider gaps in the capillary walls also facilitates the passage of immune cells from the blood into the endangered area.



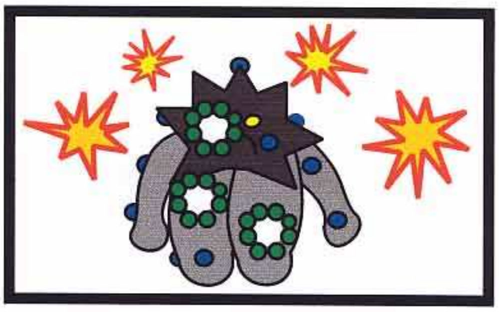


An inflammatory response will also illicit pain, as it irritates local nerve fibres.

Mast cells, macrophages and neutrophils are the most important immune cells when it comes to releasing inflammatory factors.

The T helper's role in an inflammatory response, is to overtly stimulate the macrophages and neutrophils.

COMPLEMENT AND INFLAMMATION



Complement activation leads to a localised inflammatory response.


C3a

C3a activates any nearby mast cells and causes smooth muscle cells to contract.

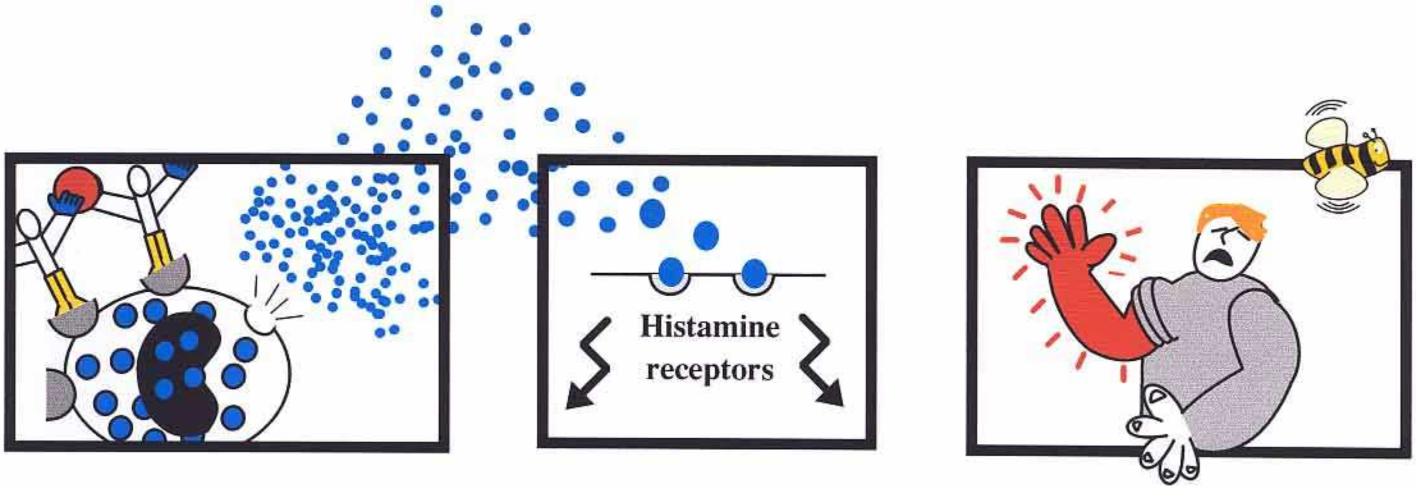

C4a

C4a has similar but a much less potent range of actions when compared to C3a.


C5a

C5a is the most potent of the 3. It activates mast cells, attracts and activates neurophils and causes endothelial cells to become 'leakier'.

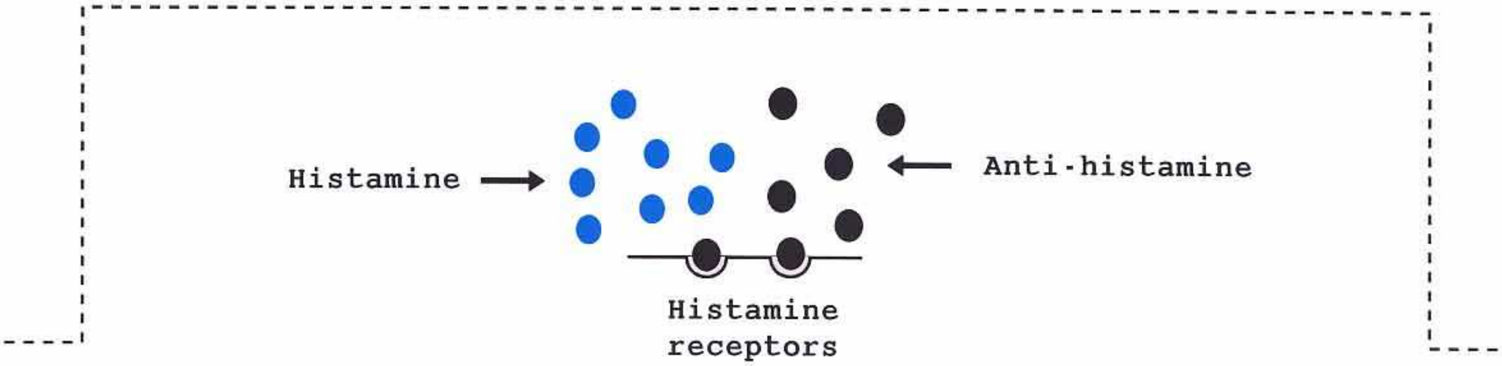
HISTAMINE



Histamine is stored in granules inside mast cells. It can then be released quickly to produce very rapid reactions.

To take effect, it must now bind onto nearby histamine receptors.

Histamine receptors are found all over the body, lining smooth muscle and endothelial cells.

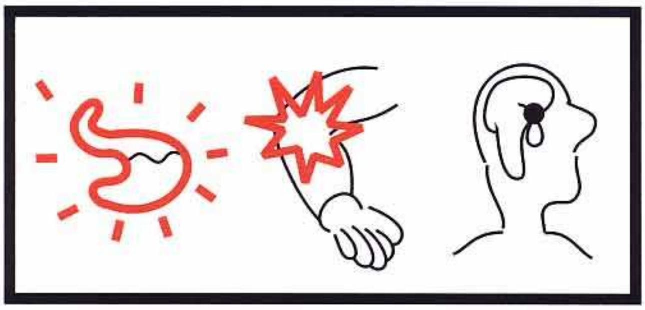


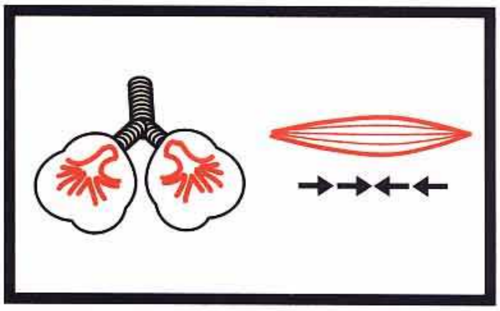
Anti-histamines fit into the histamine receptors, blocking the histamine.

But because of an imprecise fit, the anti-histamines do not activate the receptors.

PROSTAGLANDINS AND LEUCOTRIENES

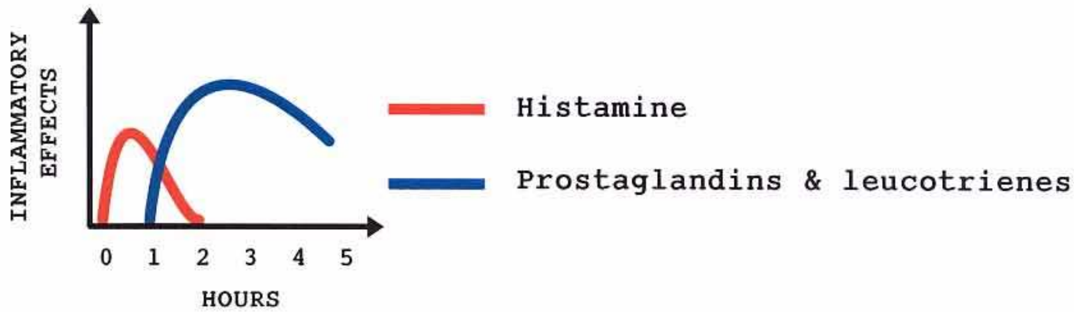
These 2 very important inflammatory mediators, can for some people, have very serious side effects.





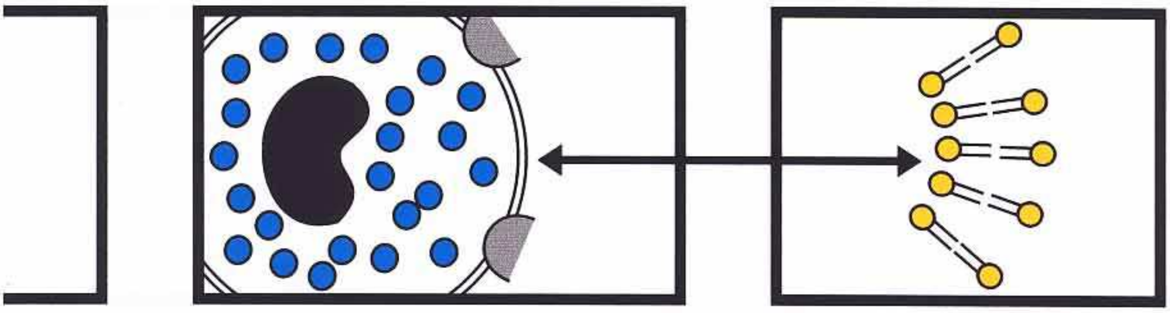
Protaglandins can trigger asthmatic attacks, joint inflammation, increase gastric acid secretion and cause the hypothalamus to raise the body's temperature.

Leucotrienes can also cause severe asthmatic attacks and very strong smooth muscle contractions.



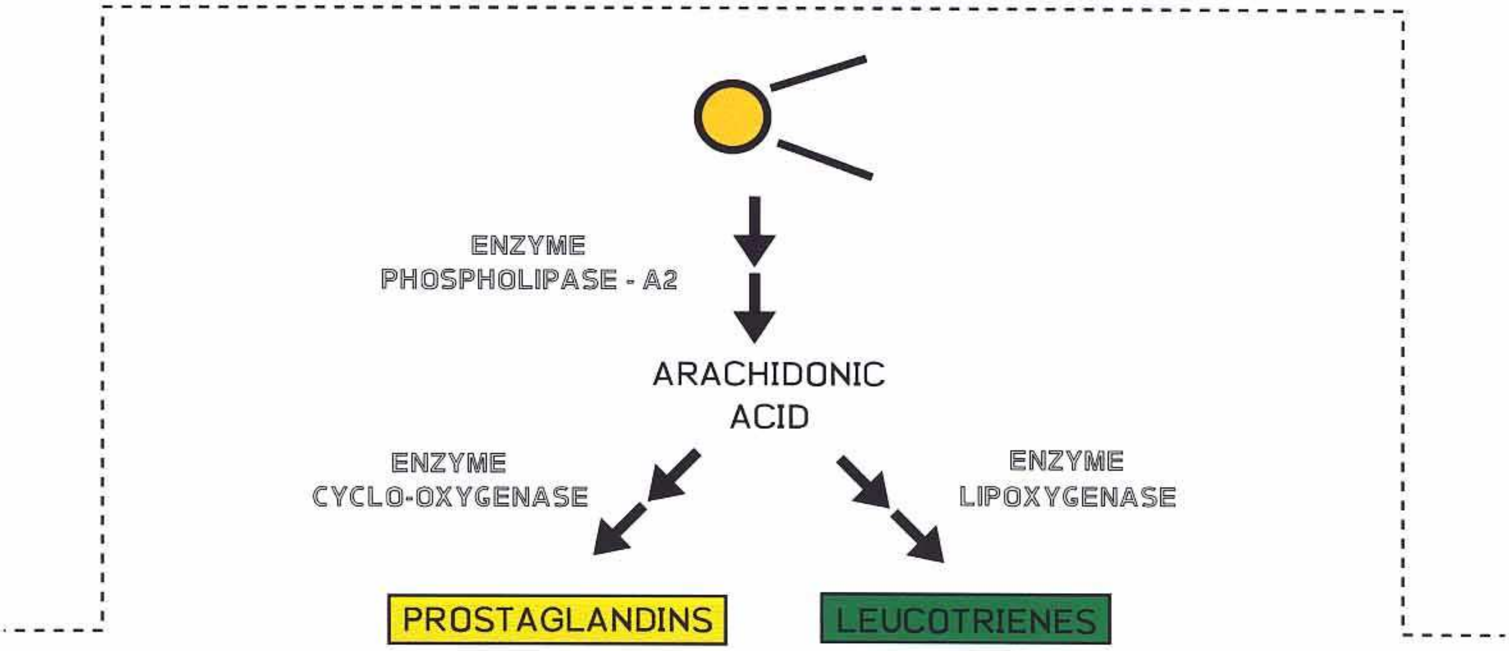
Histamine released from a mast cell, is relatively short acting. Protaglandins and leucotrienes, which are also produced by activated mast cells, are longer acting inflammatory mediators.

HOW PROSTAGLANDINS AND LEUCOTRIENES ARE MADE



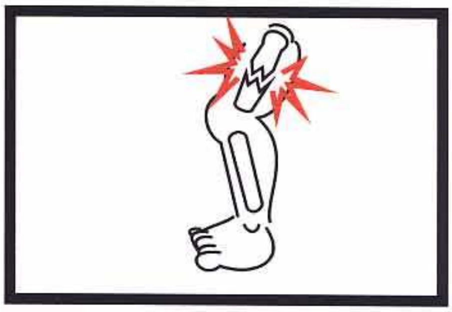
The mast cell's membrane, like all the cells in the body, is made up of a double layer of phospholipids.

Here we see a close up of the mast cell's membrane, showing the phospholipids.



Following mast cell activation, enzymes inside the mast cell, break down phospholipids into arachidonic acid and then into prostaglandins (PG's) and leucotrienes (LT's).

STEROIDS

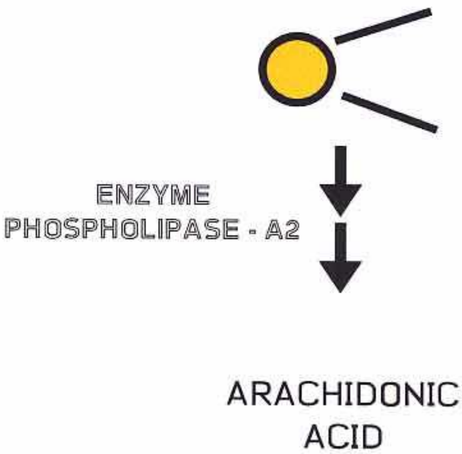


Steroids come in many forms and have some amazing anti-inflammatory properties.

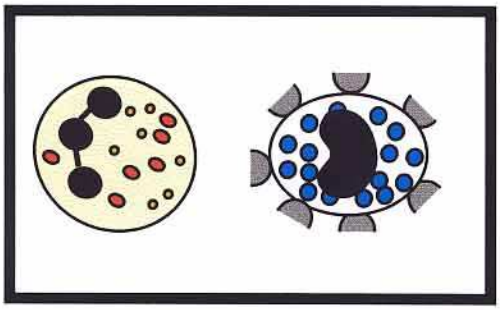
Unfortunately, there are serious side effects when they are used over a prolonged period.

Steroids prevent phospholipase-A2 from working.

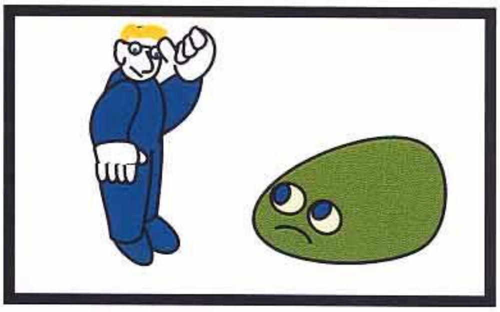
Arachidonic acid can not be made.



By stopping arachidonic acid being produced, mast cells are now unable to make prostaglandins and leucotrienes.



Steroids also prevent the release of preformed inflammatory granules.



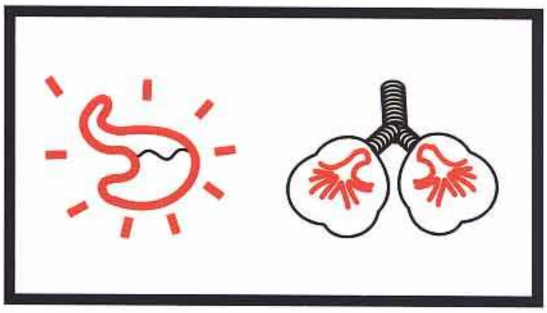
Steroids may even stop the 'attack' protein from being expressed.

Steroids work by stabalising the membranes of cells that produce inflammatory factors.

PG's and LT's can not now be produced.

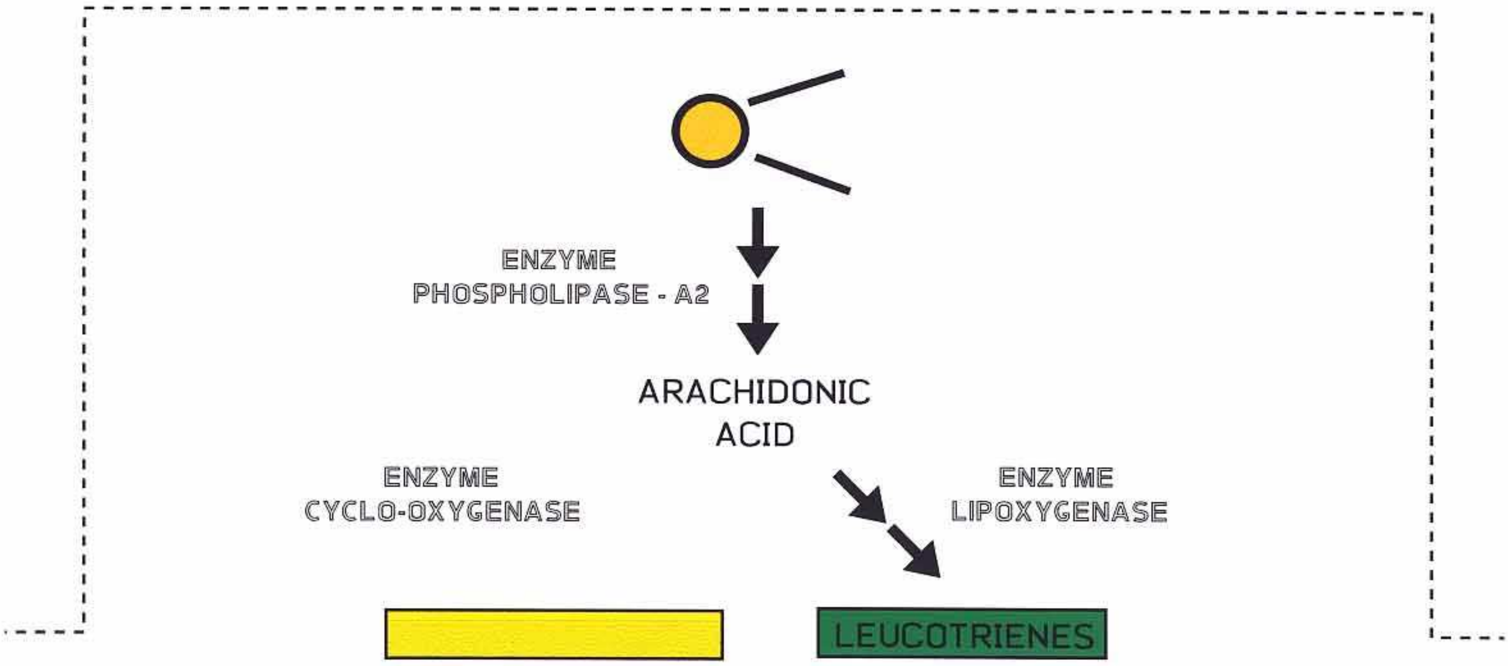
Preformed granules can not be released.

NON STEROIDAL ANTI - INFLAMMATORY DRUGS (NSAIDS)



These drugs can stop certain types of pain, because of their anti-inflammatory properties.

Unfortunately for some people, they cause problems such as gastric bleeds and severe asthmatic attacks.



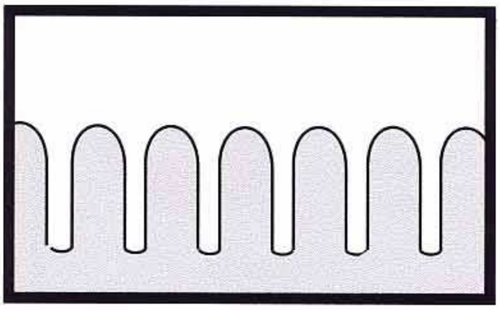
These drugs work by stopping the enzyme cyclo - oxygenase from turning arachidonic acid into prostaglandins.

However, as NSAIDS do not affect the enzyme lipoxygenase, all the arachidonic acid, is for some, now converted into leucotrienes.

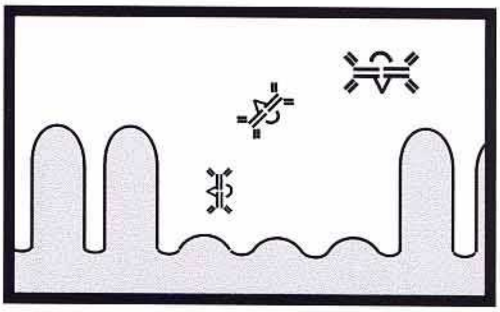
CHAPTER SIXTEEN

MISCELLANEOUS

PEYER'S PATCHES



The surface of the small intestine is lined with 'finger-like' projections called "villi".

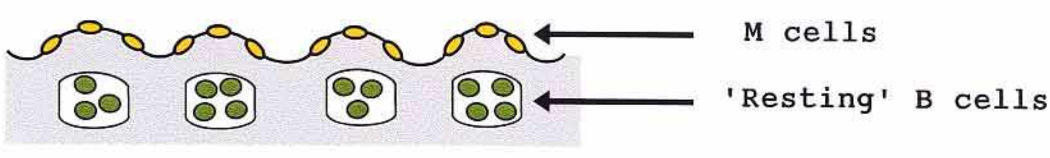


But periodically these are replaced by Peyer's patches and it is from these that IgA are released.

Easy reading

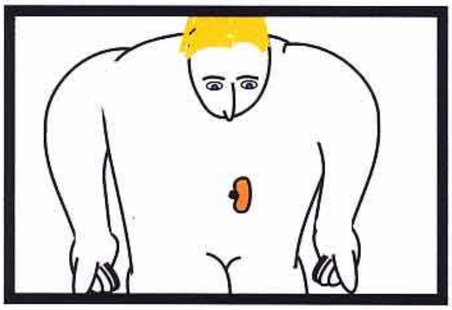
Technical information

A CLOSE-UP OF A PEYER'S PATCH

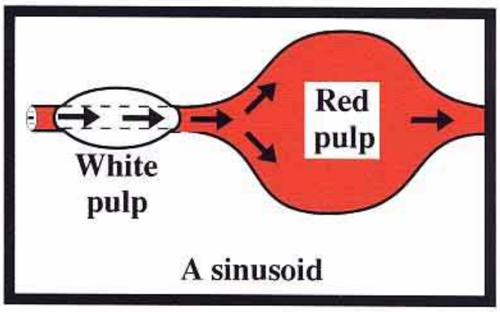


M cells allow microbes to easily penetrate the gut wall and so come into contact with the 'resting' B cells.

THE SPLEEN

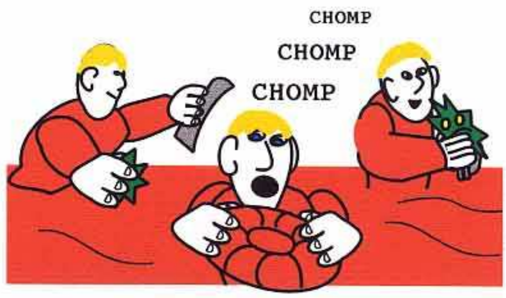


Inside the spleen, capillaries are replaced by sinusoids.



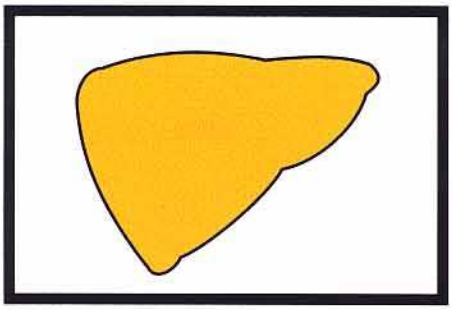
As the arteriole approaches the sinusoid, it passes through the white pulp.

The white pulp contains many B cells, which can release antibodies straight into the blood.

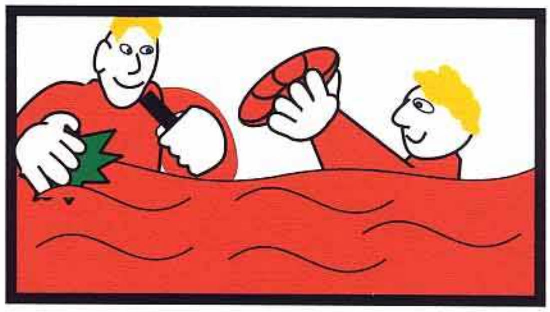


Meanwhile, in the red pulp, resident macrophages remove microbes, waste material and worn out red blood cells

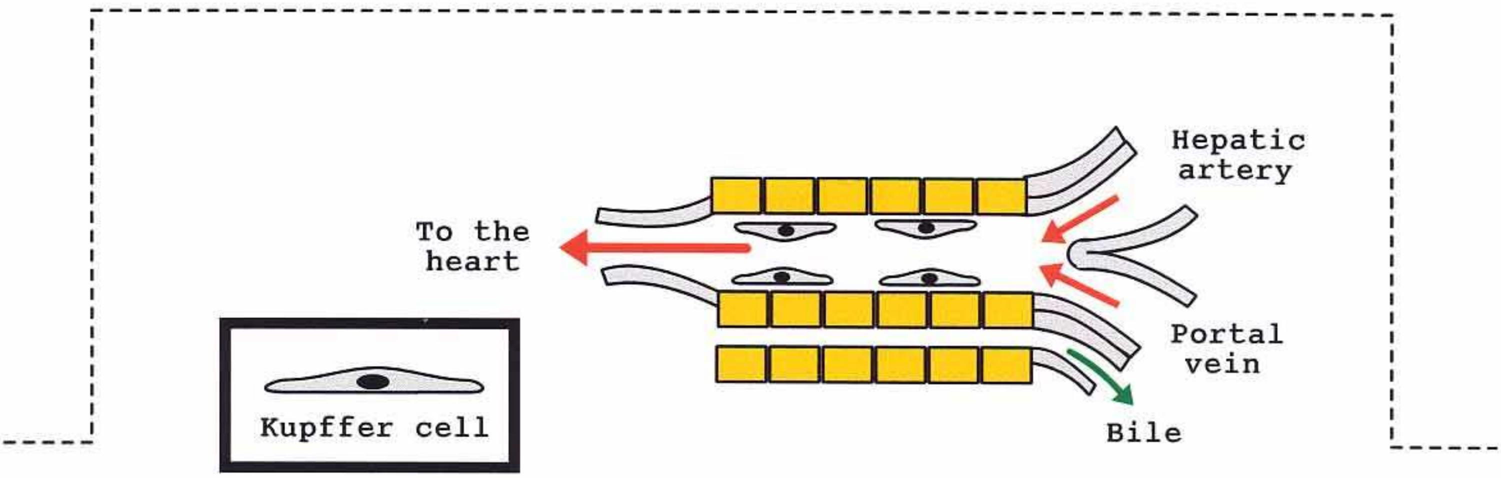
THE LIVER



The liver has many functions such as:- making bile, storing energy and detoxifying drugs.

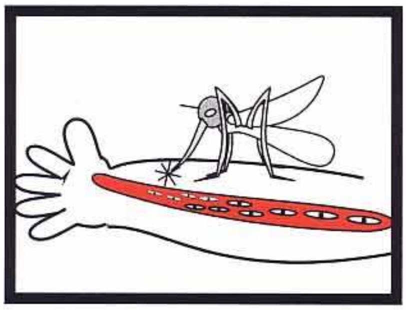


Kupffer cells (a type of macrophage found in the liver), scavenge for worn out red blood cells, microbes and waste material.

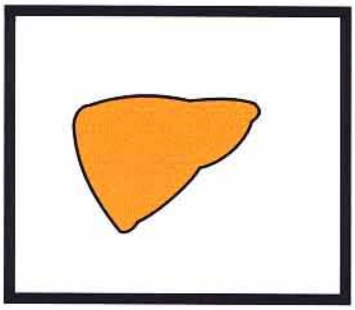


Inside the liver, capillaries are replaced by specialised sinusoids.

MALARIA



When an infected mosquito bites someone, sporozoites can enter their blood.

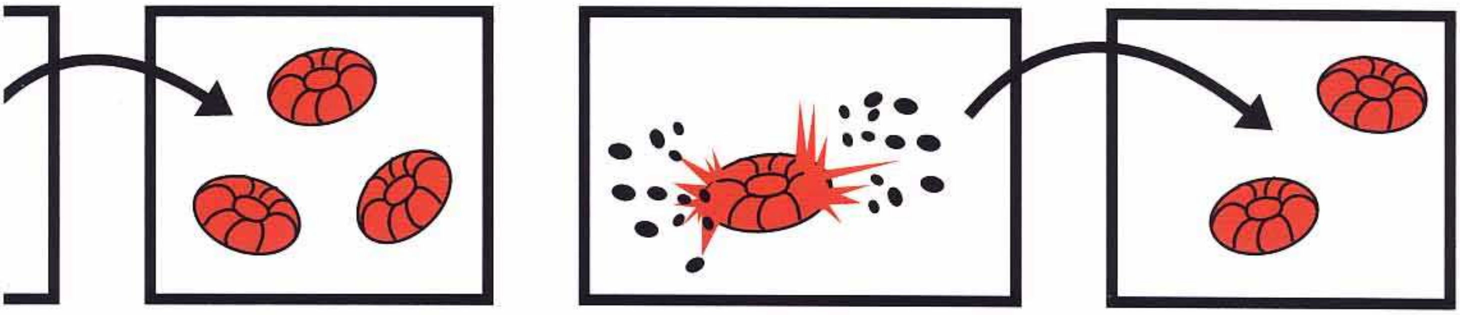


The sporozoites must now reach and infect cells inside the liver.

A couple of weeks later and merozoites burst out into the blood.

It is the anopheles mosquito which harbours the parasite responsible for causing malaria.

The parasite has a complicated life-cycle, part of which must be completed in man.

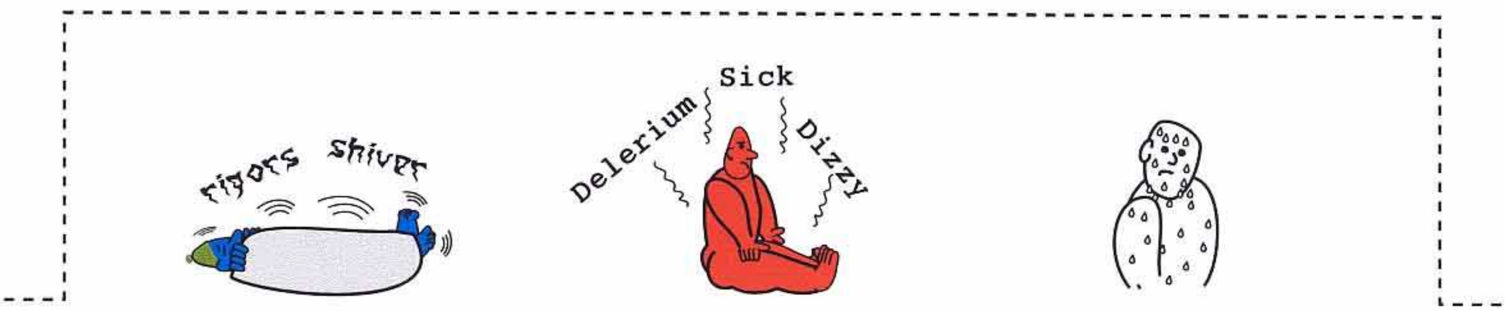


The 'exposed' merozoites, must now quickly infect other red blood cells.

After a couple of days the infected cell is filled to bursting point with many merozoites.

On entering the blood, the merozoites will infect other red blood cells.

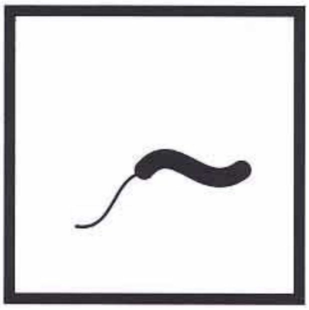
This cycle will now continue many times inside the patient.



Cold stage Hot stage Sweating stage

Each time the merozoites burst out into the blood, the patient will for a few hours, experience the classic malarial symptoms.

CHOLERA

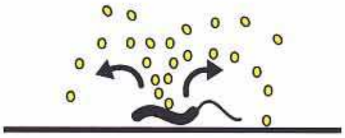


This disease is caused by the cholera vibrio.

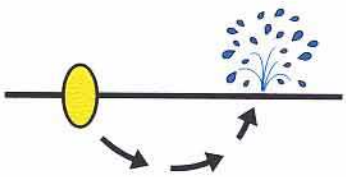
Infection usually occurs by drinking contaminated water.

Excessive 'rice water' diarrhoea now follows.

After replicating in the gut, millions of vibrios are flushed out to infect new hosts when the patient has violent diarrhoea. This is due to an excessive fluid build up, inside the bowel.

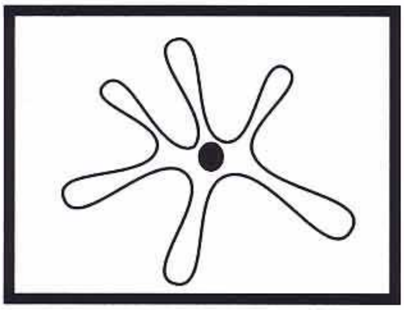


As well as replicating in the small intestine, each cholera vibrio releases enterotoxins.

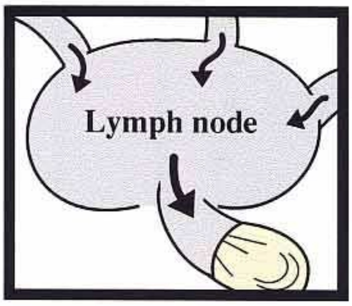


The enterotoxins pierce the gut epithelium and trigger it into releasing water and salts.

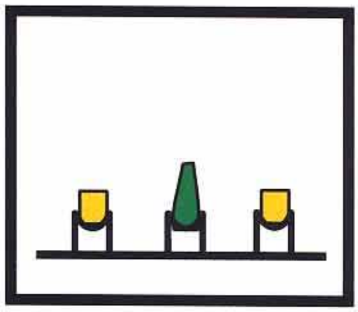
THE FOLLICULAR DENDRITIC CELL



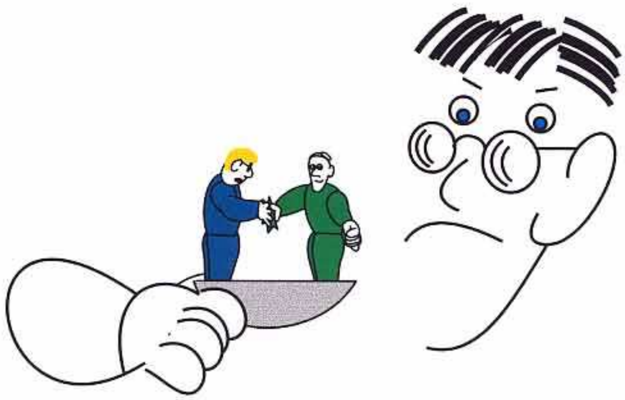
The follicular dendritic cell is found in the cortex of the lymph nodes.



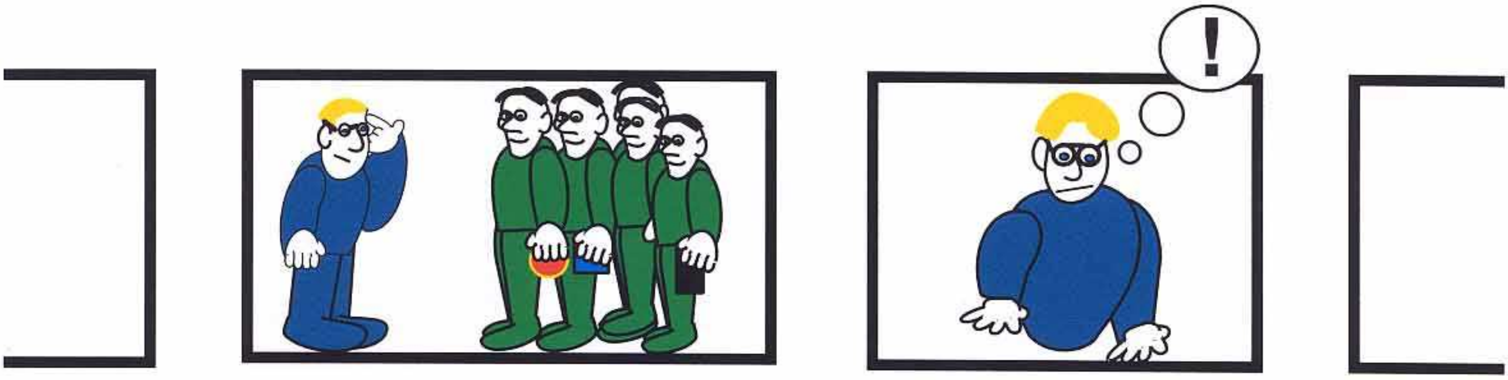
Hence they come into contact with material passing through the lymph node.



At their surface, matter will be presented, attached to 'attack' proteins.

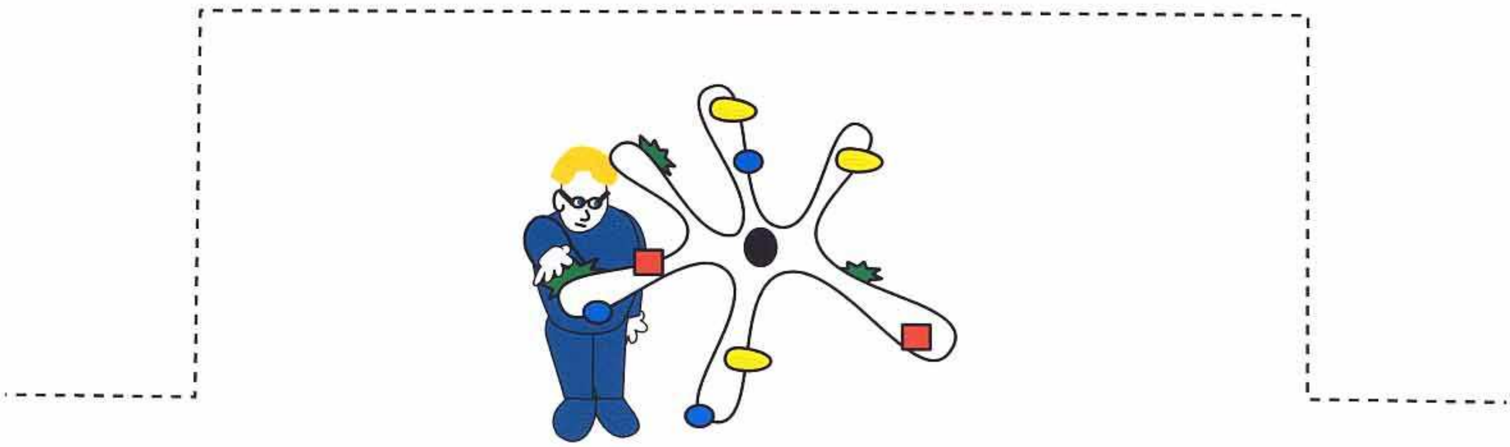


In the laboritory it is difficult to get T helper cells to stimulate B cells into producing antibodies. It appears that the follicular dendritic cells need to be present.



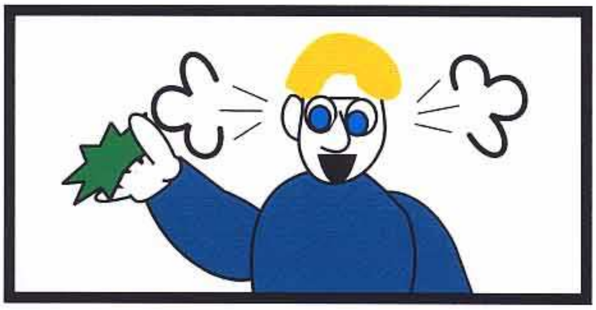
When a T helper entres a lymph node, he has to see if any of the resident B cells are presenting foreign material that 'fits' his 'hands'.

But it is difficult to see how a T helper cell can single handly check all the resident B cells.

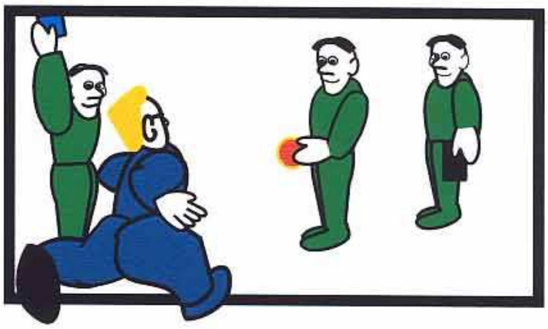


So what could happen is that when the T helper enters the a lymph node it samples all the material being expressed by the follicular dendritic cells.

THE TURNED ON T HELPER!!

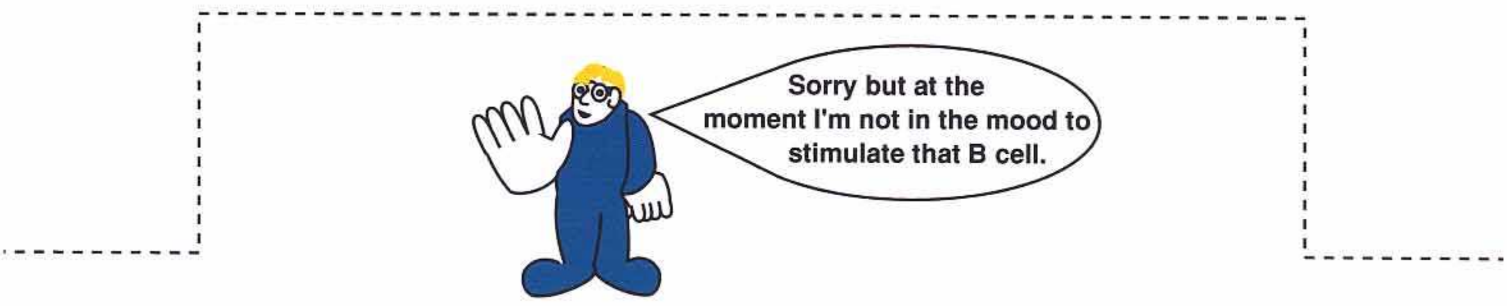


If the T helper's 'hands' fit material being expressed by a follicular dendritic cell, then this could turn the T helper on.



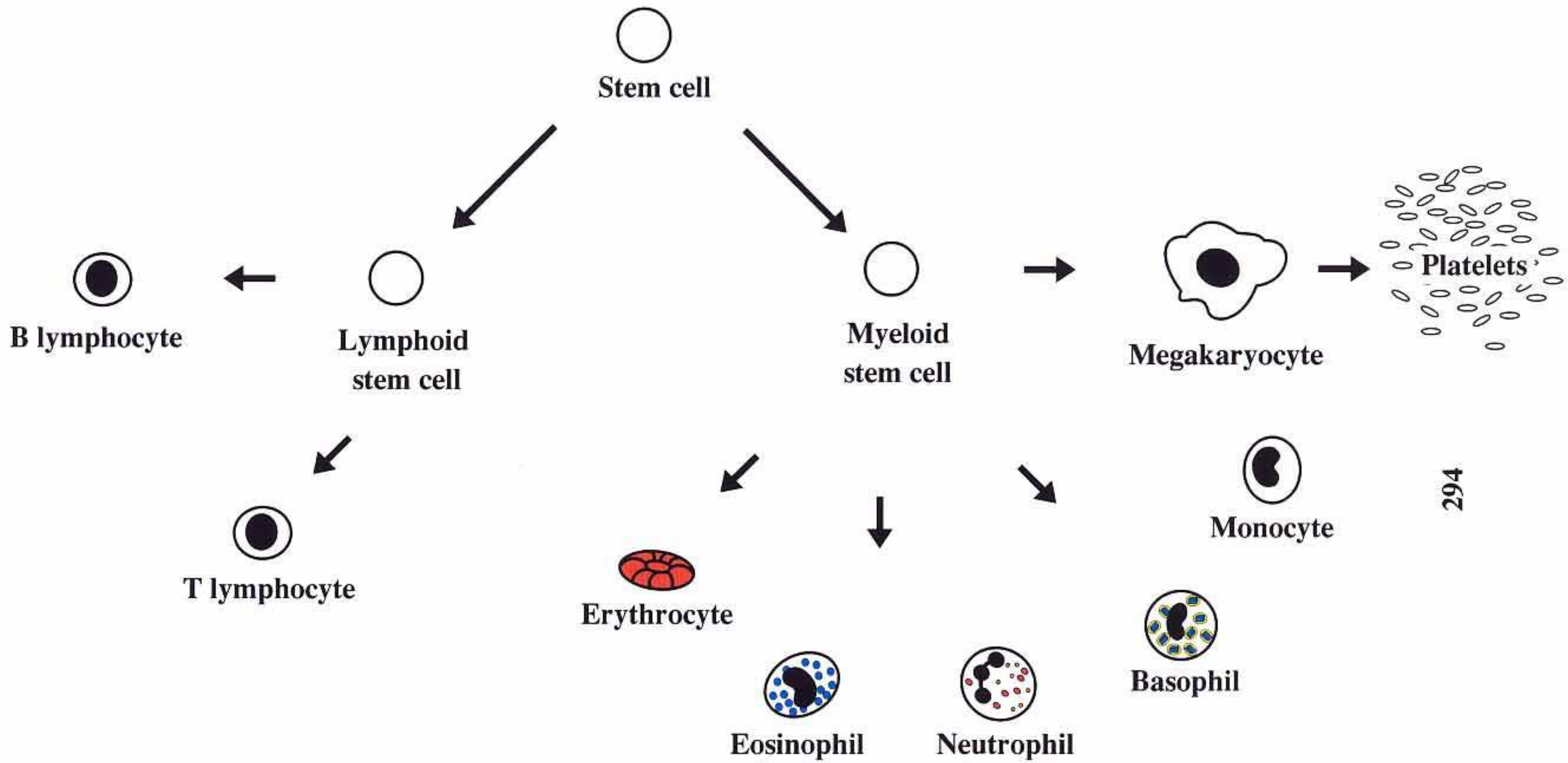
He might then search that lymph node for a B cell who is also presenting material that fits his 'hands'.

However, if the dendritic cells in the lymph node have not got anything for the T helper, then he will probably move quickly onto the next lymph node as it is unlikely that any B cell here would be presenting suitable foreign material.



So it could be that the reason the B and T helper cells will not react in the laboritory is because the T helper cell must first be turned on by a follicular dendritic cell.

THE BLOOD CELL FAMILY TREE



The bone marrow contains a pool of stem cells, each of which is capable of developing into any blood cell.

USEFUL TERMS FOR A BUDDING IMMUNOLOGIST

Accessory cell: **Any cell which expresses material attached to 'attack' proteins.**

Adjuvant: **Something which enhances an immune response.**

Agglutination: **When particulate matter is clumped together by antibodies.**

Allergen: **Any substance which triggers the release of IgE antibodies.**

Alpha interferon: **Released by virally infected cells, it appears to 'shut down' neighbouring cells in an attempt to contain the viral infection.**

Anergy: **When a B or T lymphocyte is no longer able to respond to a particular antigen.**

Antigen: **Material that is capable of triggering an antibody or T cell response.**

Antigen presenting cell: **Another way of describing an accessory cell.**

Autocrine growth factors: **When these are released (ie interleukin-2), they will trigger the cell to clone itself.**

Basophil: **This white blood cell has an S shaped nucleus, contains histamine granules and is lined with surface IgE receptors.**

Cluster determinant (CD): **A cluster of antibodies which are specific for a particular cell surface marker.**

Cytokines: **These are factors released by cells which will affect other cells.**

Delayed-type hypersensitivity: **Otherwise known as a type 4 hypersensitive reaction. Because it results from T cell activation and not does not involve antibodies, this type of reaction takes at least 24 hours to occur, following an antigenic challenge.**

Enterotoxin: A form of exotoxin, which affects the lining of the digestive tract.

Exon: A length of DNA which codes for a protein.

Farmer's lung: This and other local type 3 hypersensitive reactions, are often associated with people who work in dirty environments.

Gamma interferon: Released by T helper cells, this cytokine will overtly stimulate macrophages and neutrophils. An affected macrophage acquires a characteristic roughened membrane and may now be referred to as an 'angry' macrophage.

Granulocytes: White blood cells which contain granules (ie neutrophils and eosinophils).

'Hands': Receptors found on lymphocytes and at the ends of antibodies, which have a unique fixed shape.

Histocompatibility: A transplants ability to survive inside a recipient.

Interleukins: Factors which allow white blood cells to 'communicate' with each other.

Interleukin-1: Released by macrophages, it has a wide range of actions, one of which is to act as a second signal to T helper cells (see page 88).

Interleukin-2: Released by T helper cells, this cytokine will affect other immune cells in the vacinity and also act as an autocrine growth factor.

Intron: A non coding length of DNA.

Isotype: This word is referring to an antibody's class (ie IgA, IgE etc).

Leucocyte: A white blood cell.

Lymphokine-activated killer cells (LAKs): When NK cells are exposed to a high concentration of interleukin-2, they transform into LAK cells, which appear to possess enhanced anti-cancer and anti-viral properties.

Macrophage-activating factor (MAF): **Released by T helper cells, this cytokine enhances a macrophage's ability to breakdown phagocytosed material and to upgrade its release of inflammatory factors.**

Migration inhibition factor (MIF): **Released by T helper cells, this cytokine encourages macrophages to remain at a particular location.**

Mucosa-associated lymphoid tissue (MALT): **Peyer's patches, the adenoids and tonsils and mesenteric lymph nodes are all part of MALT. From these, IgA are released into the respiratory and gastrointestinal tracts.**

Natural killer cell (NK cell): **A type of lymphocyte that has surface IgG receptors but lacks T cell receptors. Although their function in health remains obscure, they appear to possess anti-cancer and anti-viral properties.**

Opsonins: **When antibodies or complement C3b coat the surface of a microbe to facilitate phagocytosis, they are called "opsonins".**

Perforin: **Released by NK cells onto the surface of a target cell, perforin molecules will insert into the membrane before polymerising into MAC-like complexes.**

Polymorphonuclear leucocytes: **Otherwise known as neutrophils, due to their multi-lobed nucleus.**

Transforming growth factor: **Released by macrophages and T helper cells, this cytokine switches off an immune assault and initiates tissue repair.**

T cell Receptor (TcR): **This specifically refers to the CD3 and Ti molecules.**

Thymus gland: **Although this organ is vital for T cell maturation, it starts to undergo involution once an individual reaches adolescence.**

Vascular cell adhesion molecules: **Endothelial cells can be triggered into expressing a range of adhesion molecules. Passing immune cells will attach onto these, before then migrating from the blood vessel into the tissues.**

BIBLIOGRAPHY

Allergy: Arshad
Churchill Livingstone

Anti microbial drug action: Williams et al
Blos Scientific Publishers

Atlas of immunology: Cruse et al
Springer

Basic & clinical immunology: Peakman et al
Churchill Livingstone

Basic pathology (7th edition): Robbins et al
Saunders

BNF:
Pharmaceutical Press

Case studies in immunology: Rosen et al
Garland

Cell biology: Pollard et al
Saunders

Cellular & molecular immunology (5th edition): Abbus et al
Saunders

Clinical Immunology (4th edition): Chapel et al
Blackwell Science

Clinical immunology & serology: Stevens
Davis

Essentual histology: Cormack
Lippincott, Williams & Wilkinks

Essentuals of allergy: Krishna et al
Martin Dunitz

Focus on human biology: Rischer et al
Harper Collins

Haematology at a glance: Mehta et al
Blackwell Science

Histopathology & cell biology: Kierszenbaum
Mosby

How the immune system works (2nd edition): Sompayrae
Blackwell Publishing

Immunology... A short course (second edition): Benjamini et al
Willey - Liss

Immunology (2nd edition): Klein et al
Blackwell Science

Immunology(5th edition): Goldsby et al
Freeman

Immunology 6th edition: Roitt et al
Mosby

Immunobiology 5: Janeway et al
Churchill Livingstone

Immunology at a glance 7th edition: Playfair et al
Blackwell Science

Immunology for medical students: Nairn
Mosby

Immunology, immunopathology & immunity (6th edition): Sell
ASM press

Immunology nomenclature: Editor M Turner
Hogrefe & Huber

Infectious Diseases in 30 days: Southwick
McGraw Hill

Medical immunology (10th edition): Parslow et al
McGraw Hill

Medical microbiology (2nd edition): Barton
Addison Wesley

Medical pharmacology at a glance: Neal
Blackwell Scientific

Practical immunology (4th edition): Hay
Blackwell Science

Pathology illustrated: Govan et al
Churchill Livingstone

Really essentual medical immunology: Roitt et al
Blackwell Science

The physiology of the excitable cell 4th edition: Aidley
Cambridge University Press

Tuberculosis: Editors Porter & Grange
Imperial College Press

INDEX