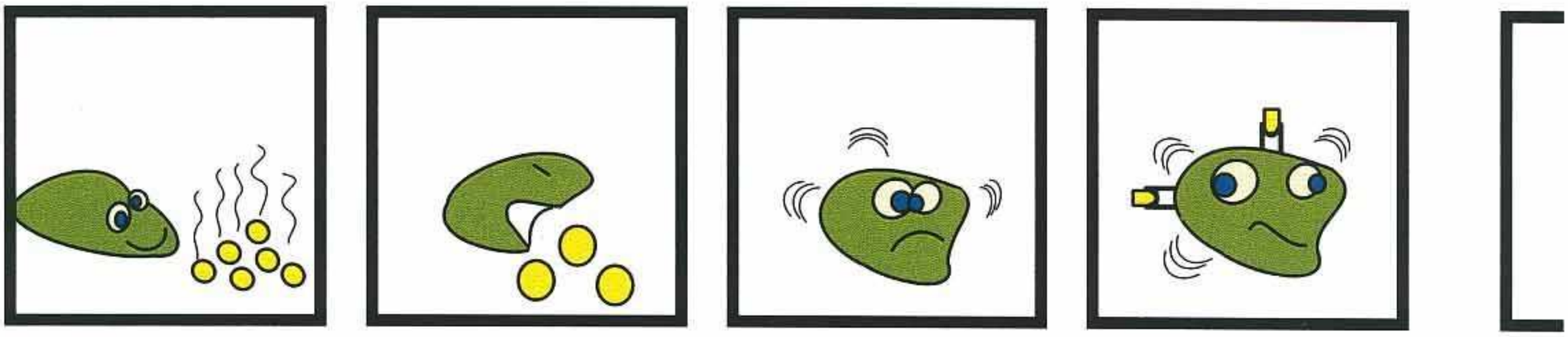
CHAPTER THREE

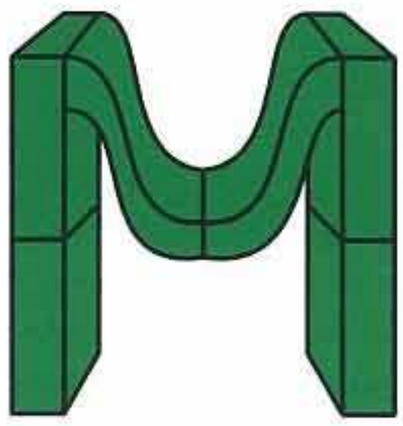
THE 'ATTACK' PROTEIN



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'.

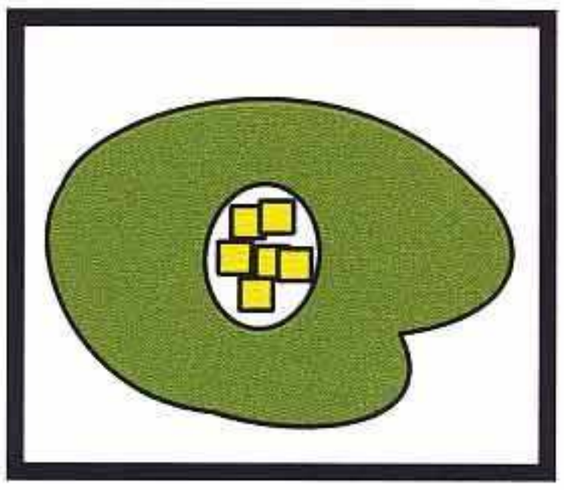
Easy reading

Technical information

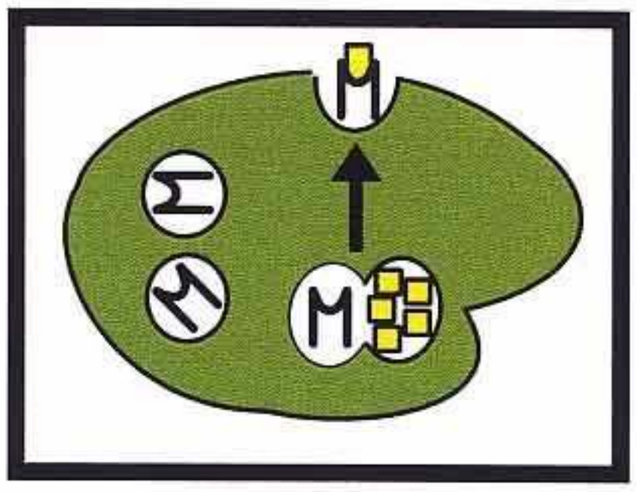


The 'attack' protein's technical (offical) name is the major histocompatibility complex (MHC) class 2 protein.

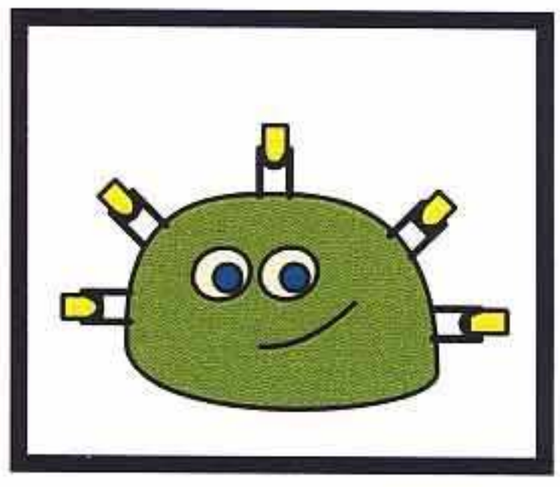
PRESENTING HIS WEARS



Enzymes start breaking down the 'eaten' material.



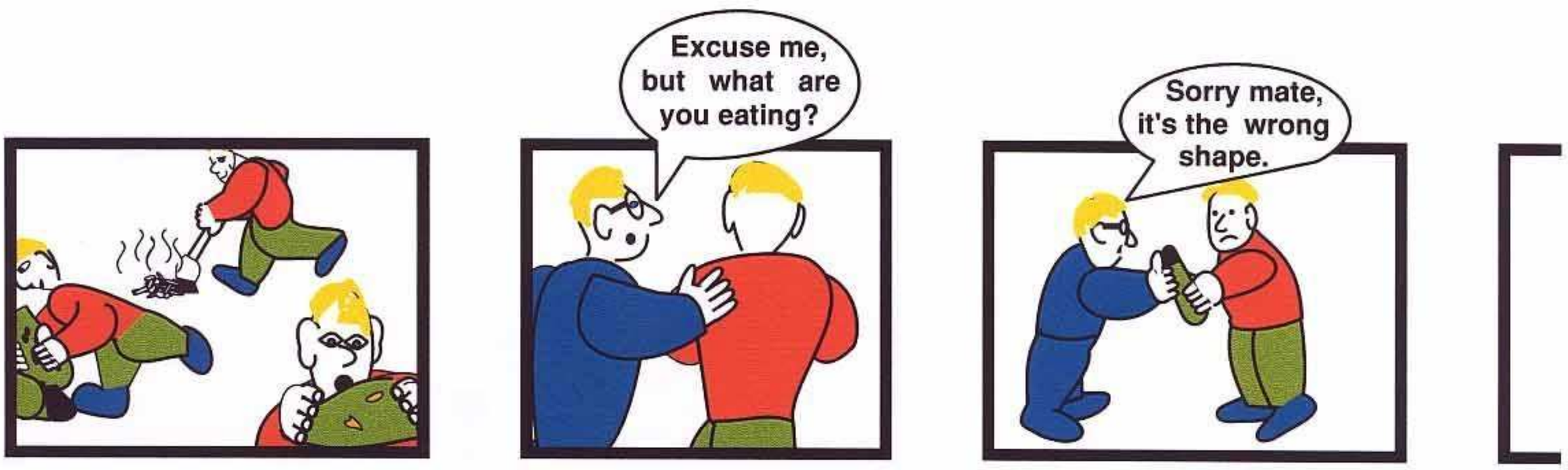
Some of the degraded material is now 'slotted' into the top of the 'attack' proteins.



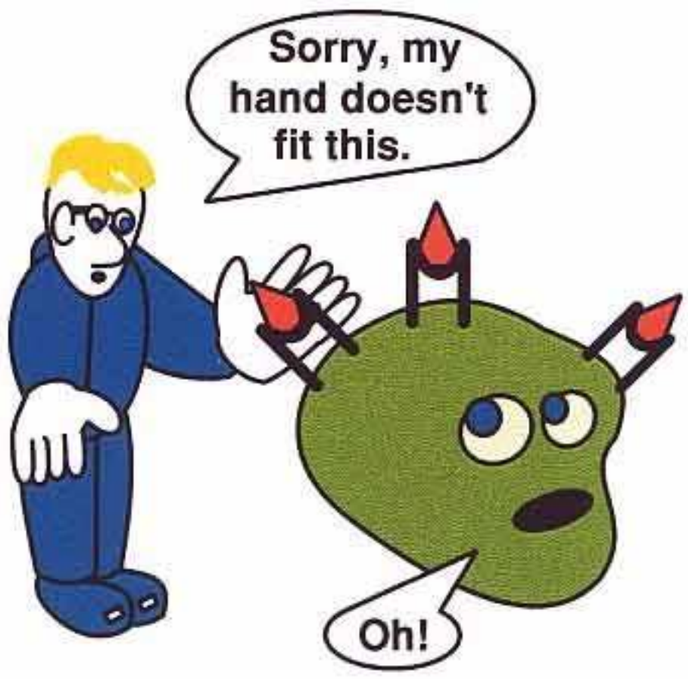
The complexes are then expressed onto the surface of the cell.

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

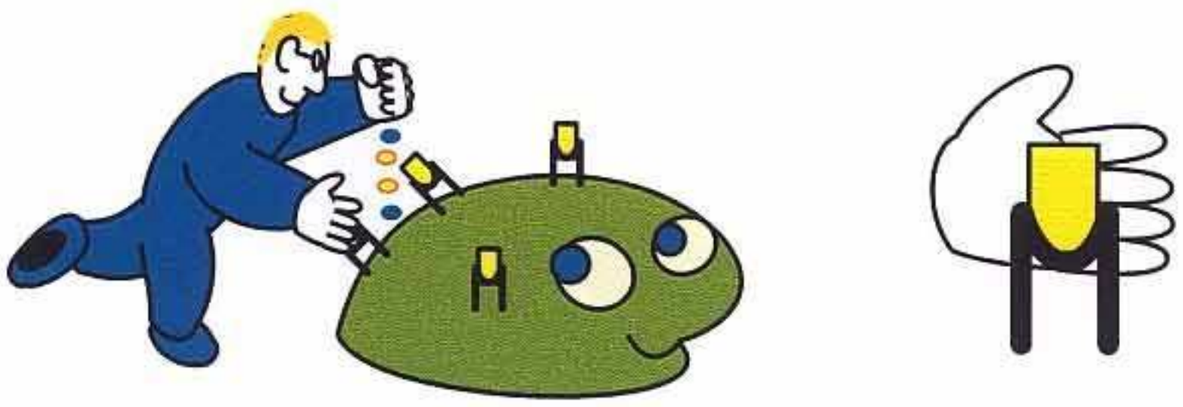


As these macrophages dispose of some waste material, a T helper arrives to see if he can help.

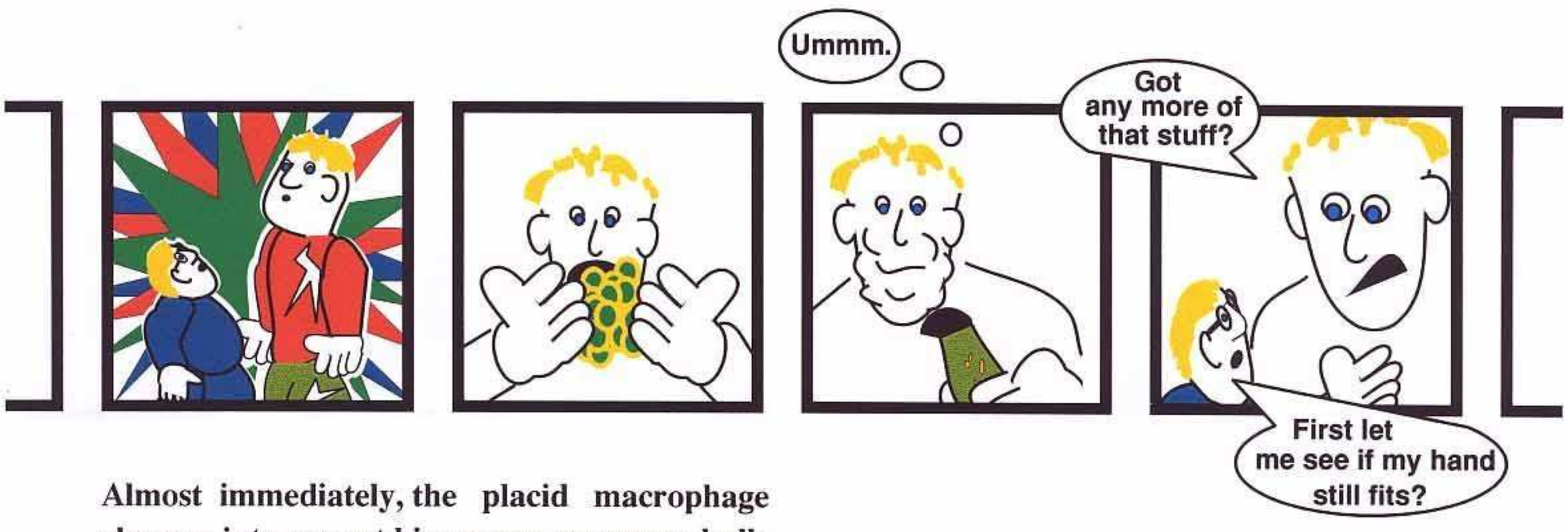


T helper cells can only help if their fixed 'hand' shape fits the presented material.

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

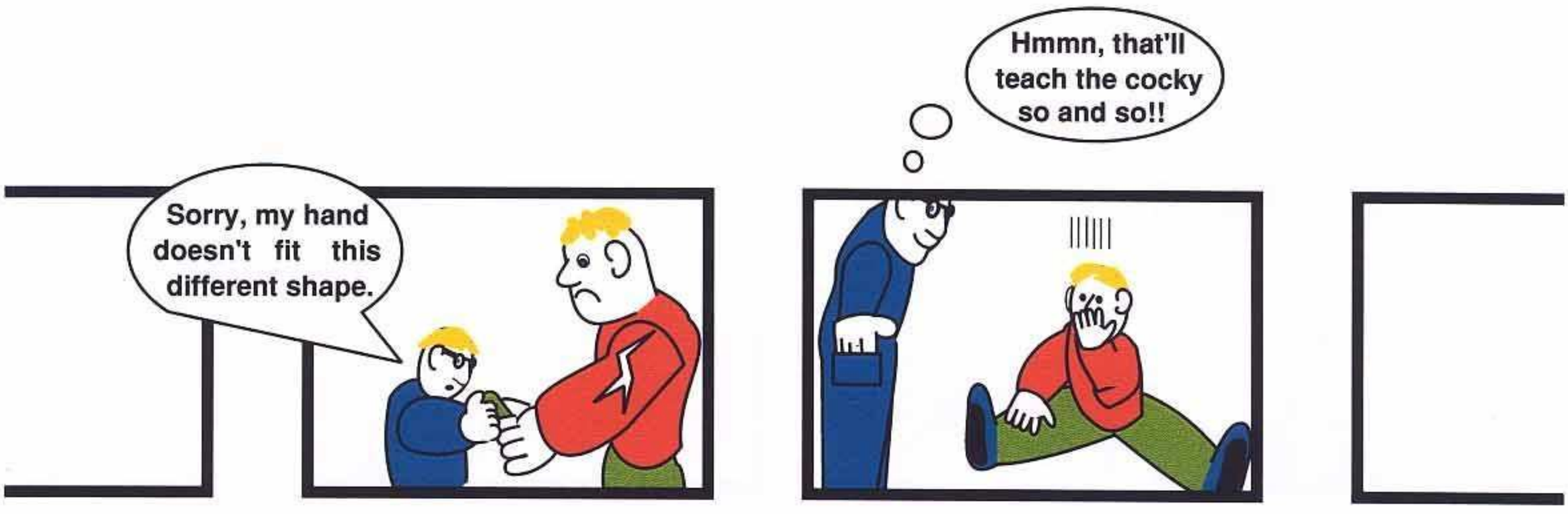


When his 'hand' does fit, the T helper releases cytokines such as:- gamma interferon, interleukin-2, macrophage activation factor and migration inhibitor factor (see page 297).

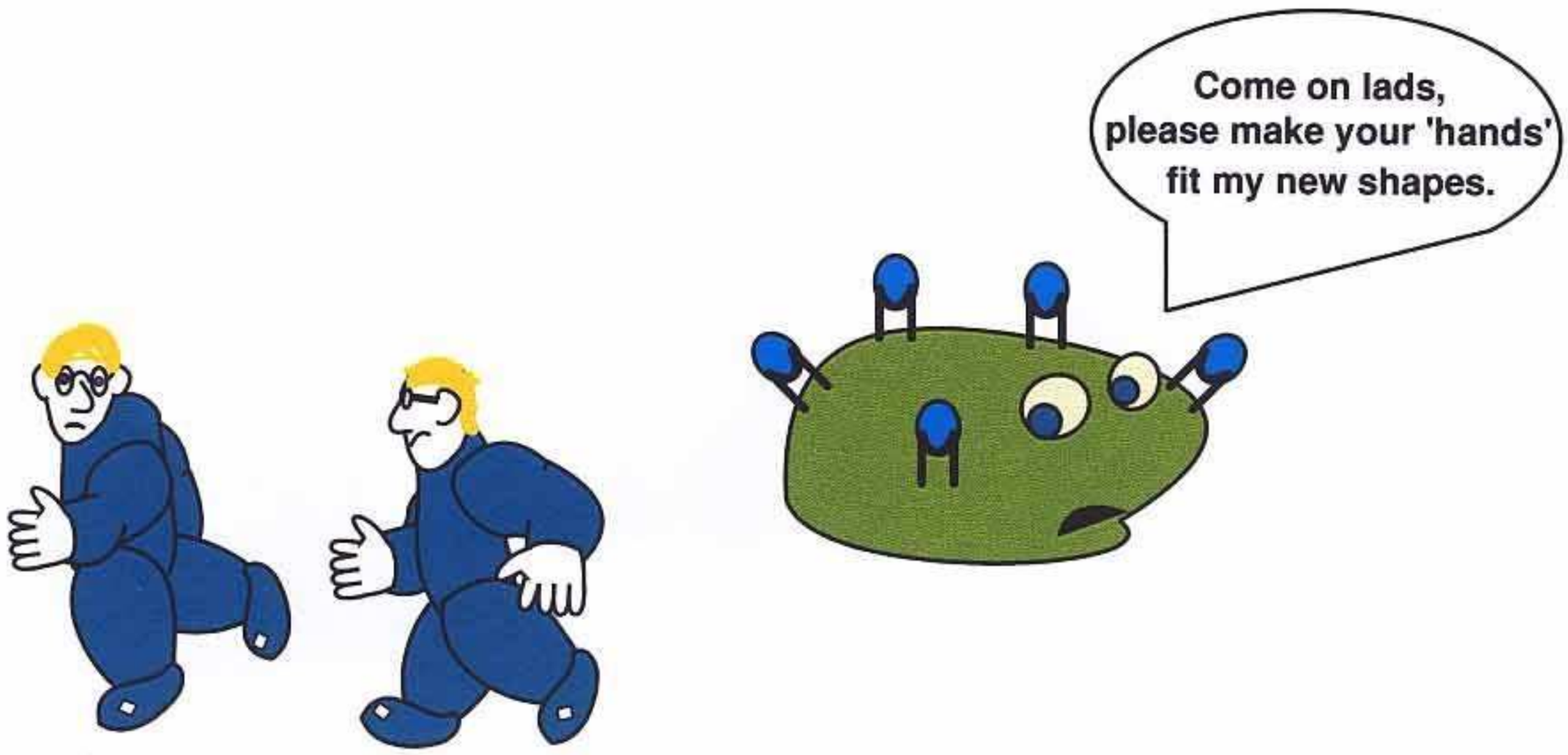


Almost immediately, the placid macrophage changes into a great big, angry, ravenous, hulk.

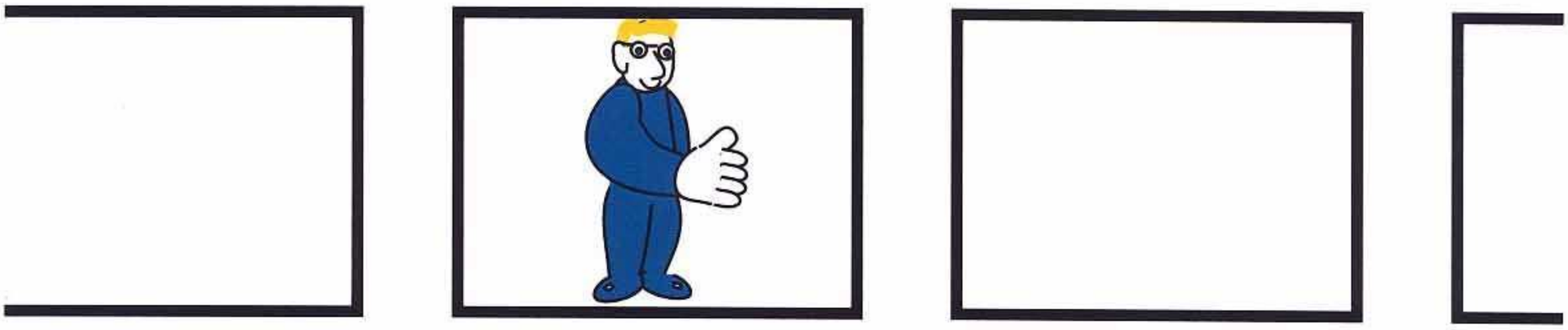
Cytokines from the T helper not only make any macrophages close by very 'angry' and much more efficient at killing microbes, but they also enable the T helper cell to clone itself.



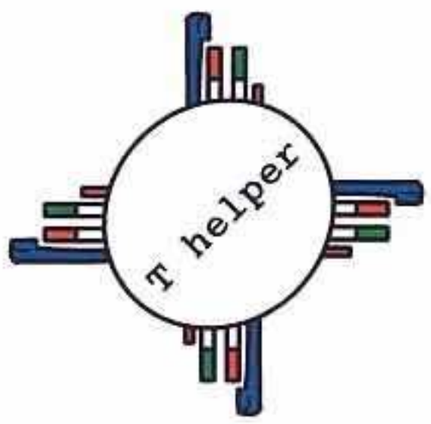
Unfortunately for the macrophage, the effects are only short lived. So once the material has been removed, he will not receive any further stimulation and quickly returns to normal.



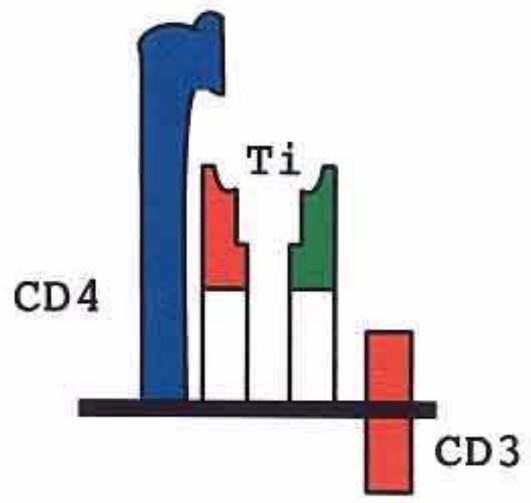
As these T helper clones have identically shaped 'hands', neither can help the macrophage, as it is now expressing a different shaped protein, attached to its 'attack' proteins.



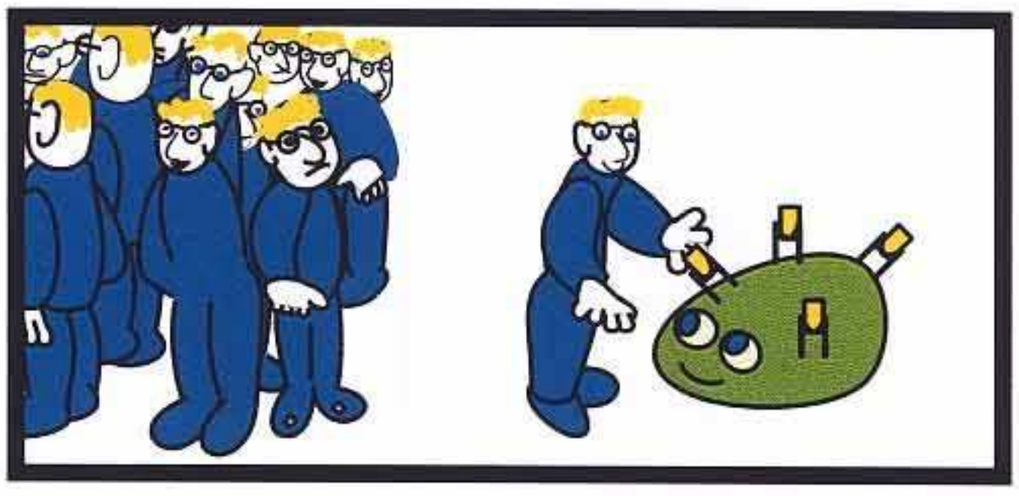
Let's have a closer look at this T helper cell's 'hand'.



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

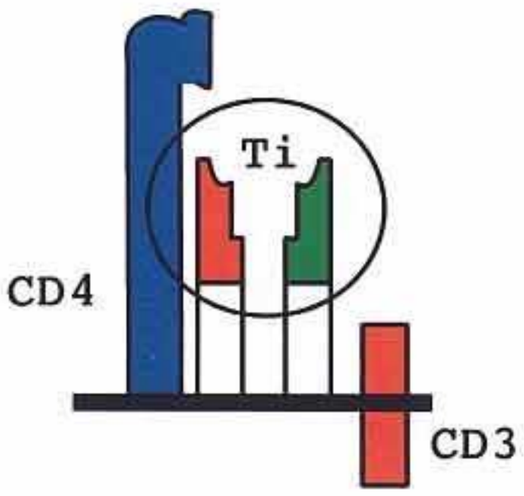


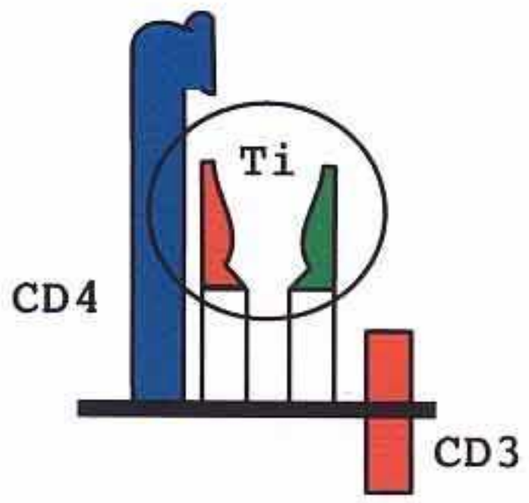
Each 'hand' is made up of a Ti, CD3 and CD4 molecule.



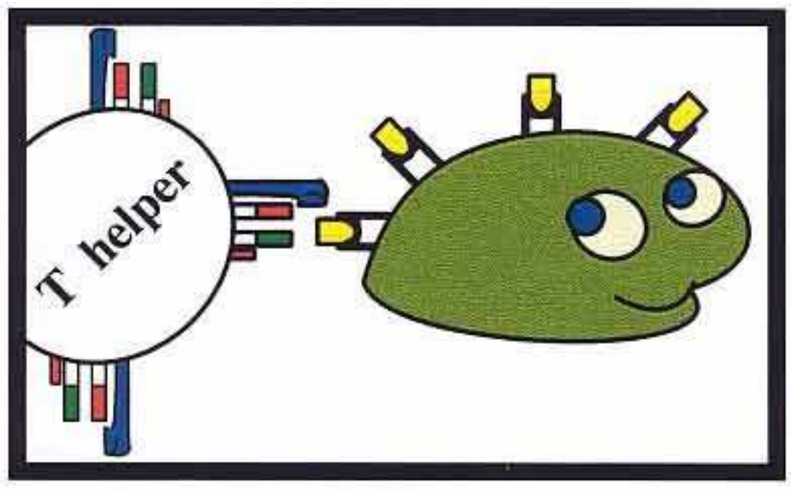
If all these T helper cells have 'hands', why has only one of them been able to 'grab' hold of what this macrophage is presenting?

2 T HELPER CELL 'HAND' SHAPES

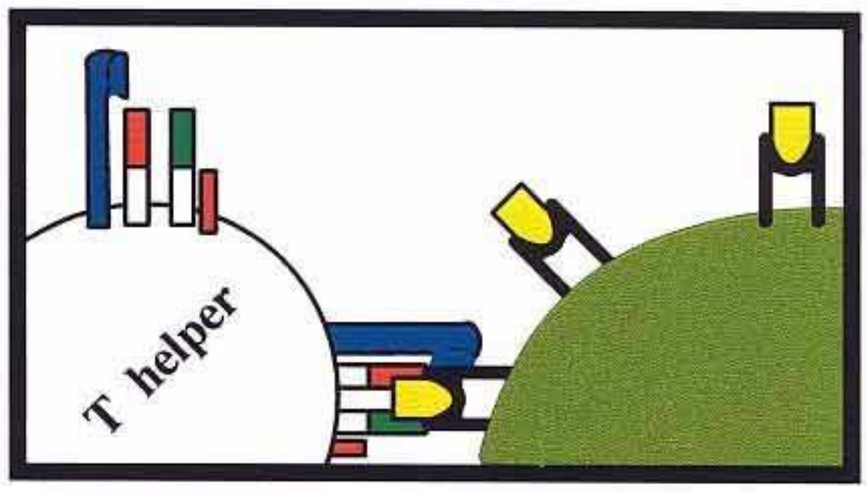




Although all T helpers have 'hands' (ie CD3, CD4 and Ti molecules) each has a unique shape at the end of their Ti molecule. It is this which greatly restricts what will fit into its 'hand'.

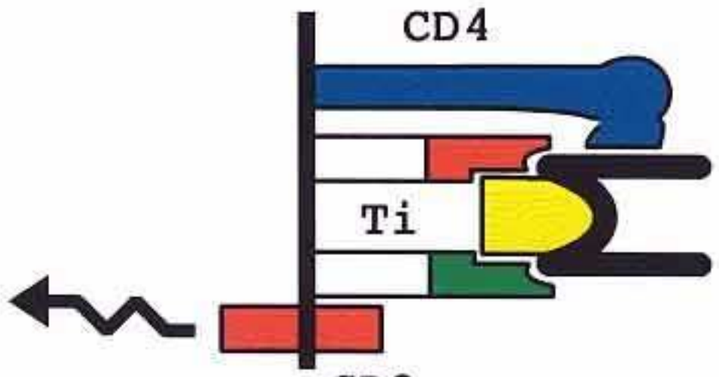


Will this T helper cell's 'hand', fit what the macrophage is presenting?



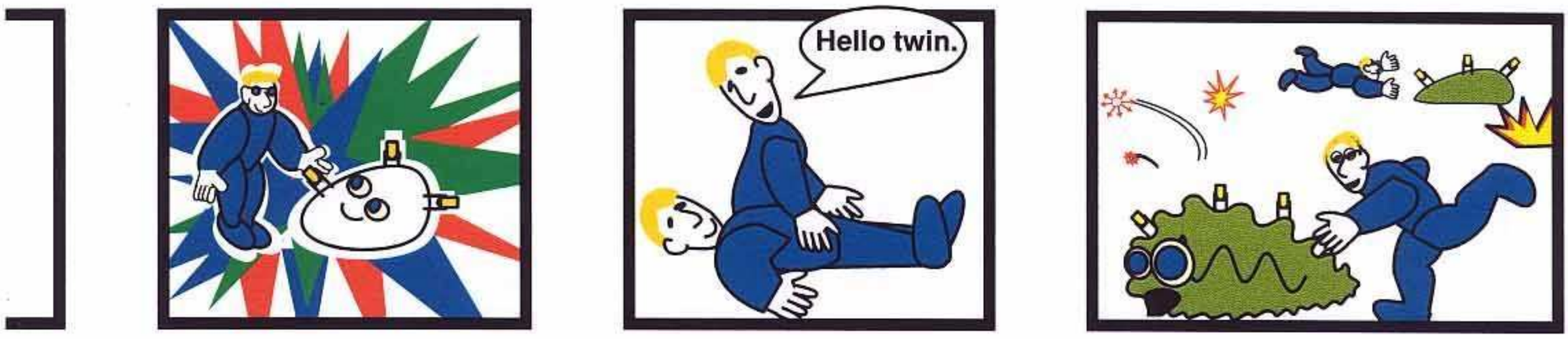
Yes, it's 'hand' fits!!

FOR THAT PERFECT FIT

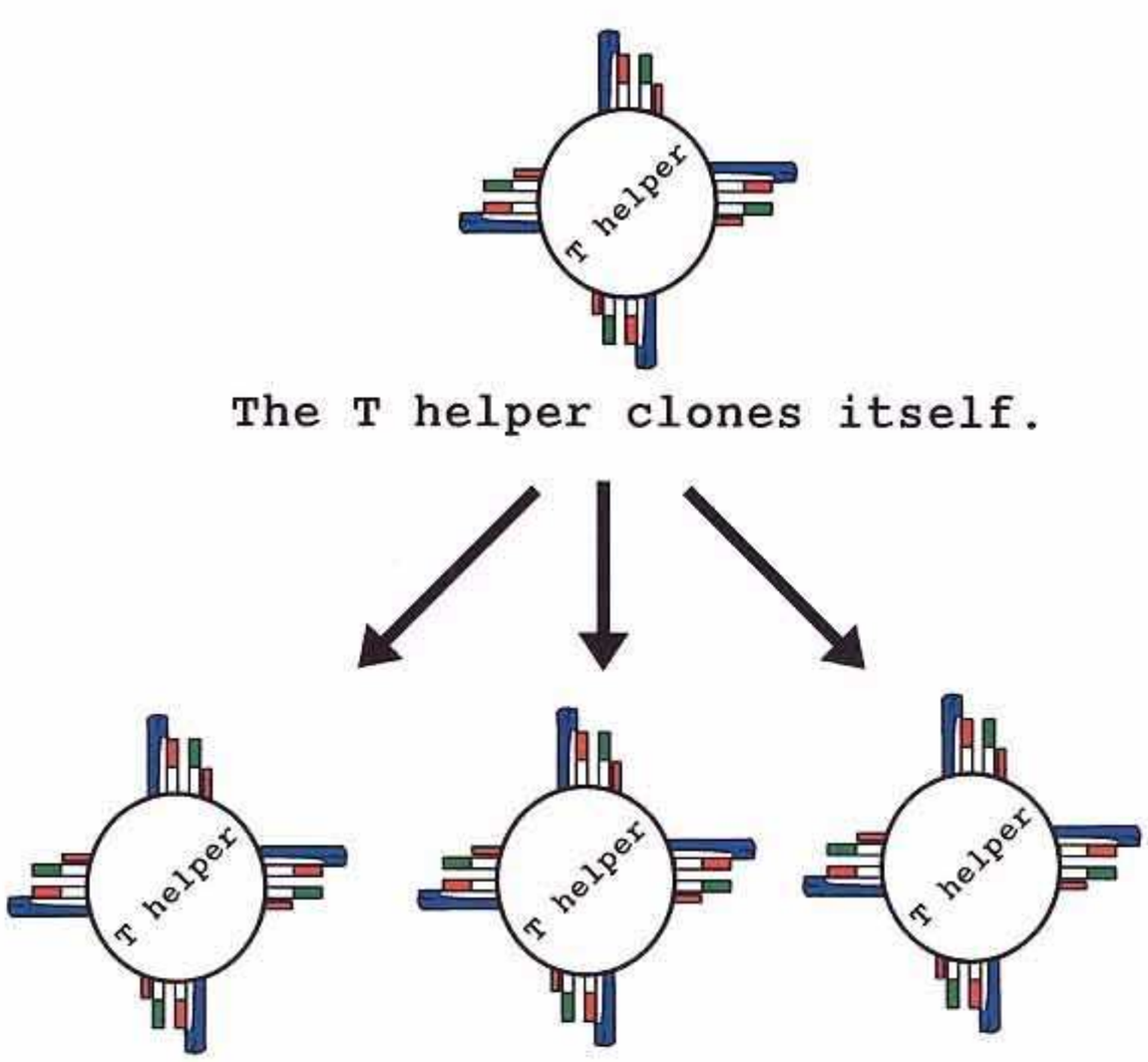


1. CD4 attaches to the side of the 'attack' protein.
2. Ti fits over the top of the 'attack' protein + foreign protein.
3. CD3 can now signal to the nucleus that the 'hand' fits.

ANOTHER EXAMPLE OF THE CLONAL SELECTION THEORY

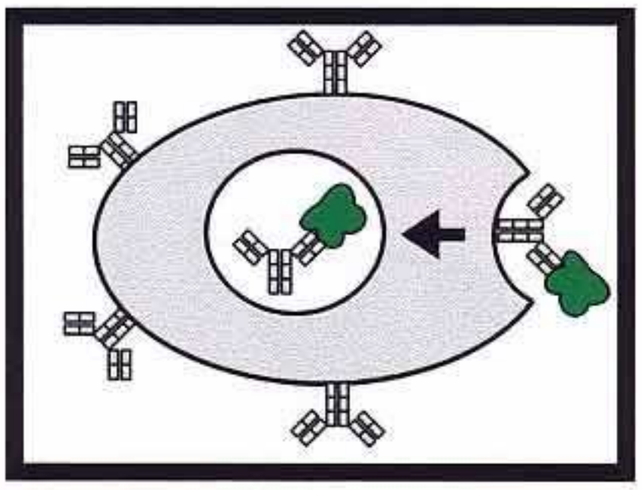


When a T helper's 'hand' fits the presented material, it releases cytokines. These cytokines not only activate any macrophages that are close by, but they also enable the T helper to clone itself.

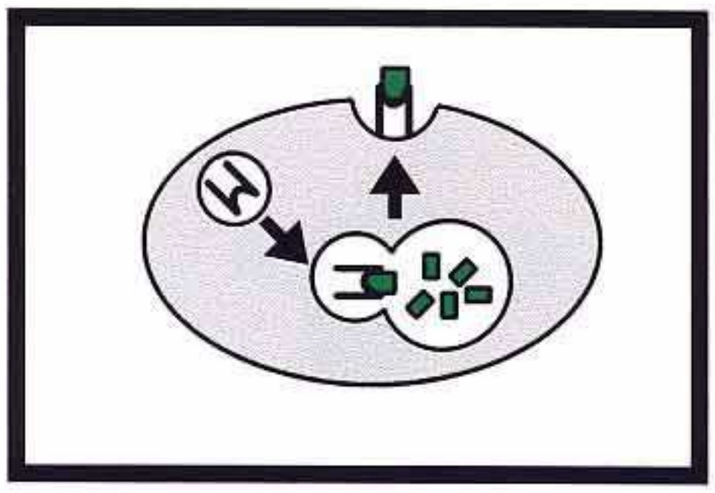


These clones have the same shaped 'hands' as the original T helper. So there are now many more T helper cells ready to respond, should the same foreign material attached to 'attack' proteins reappear.

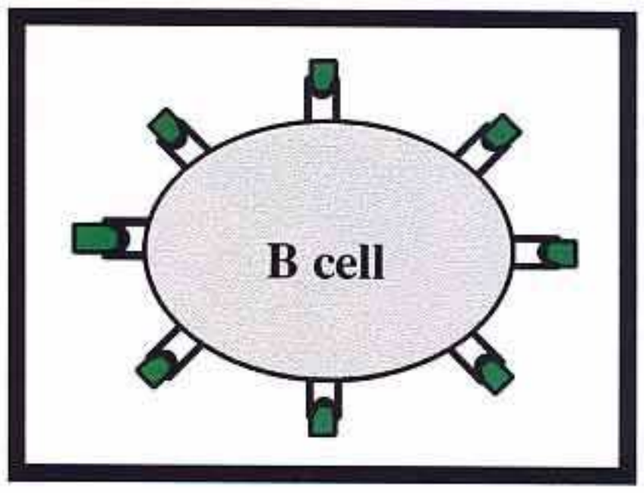
B CELLS AND THE 'ATTACK' PROTEIN



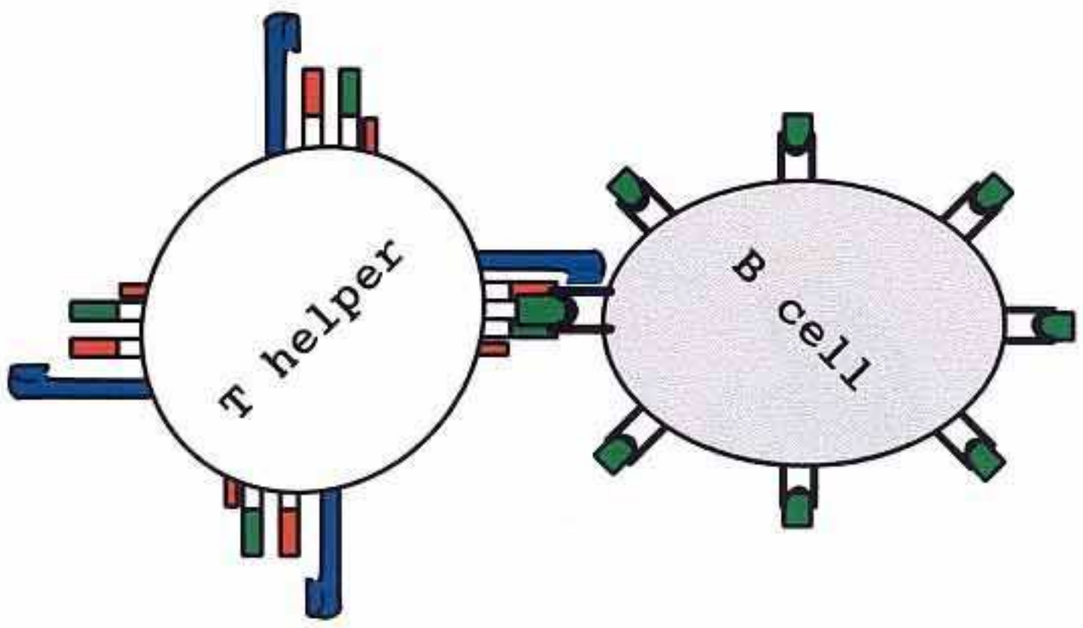
A passing piece of matter attaches onto one of this B cell's surface antibodies.



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

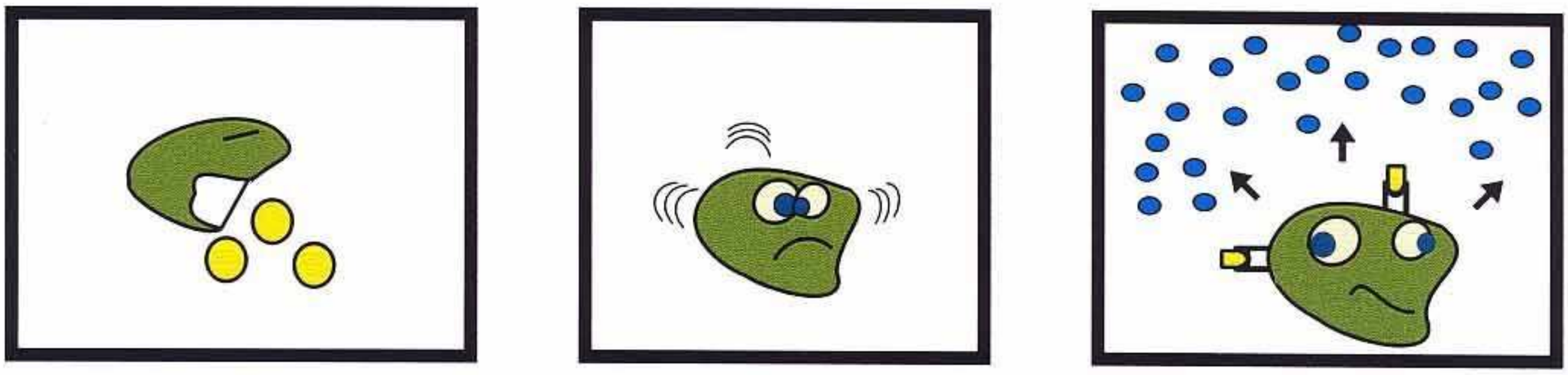


These complexes are now expressed onto the surface of the B cell.

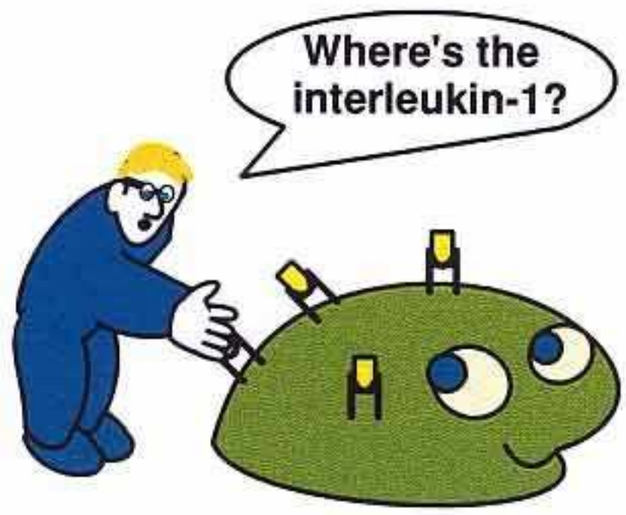


Here we see a T helper with the right shaped Ti receptor. Apart from macrophages and B cells, few other cells in the body routinely express the 'attack' protein.

THE SECOND SIGNAL

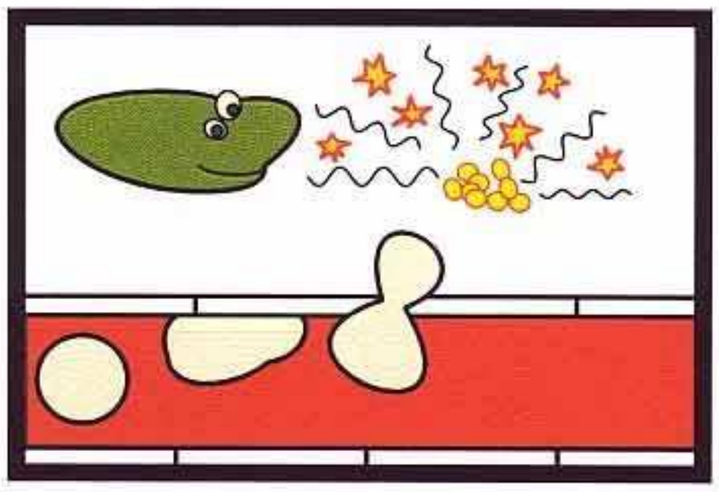


When material is expressed onto their surface, macrophages should also release interleukin-1.



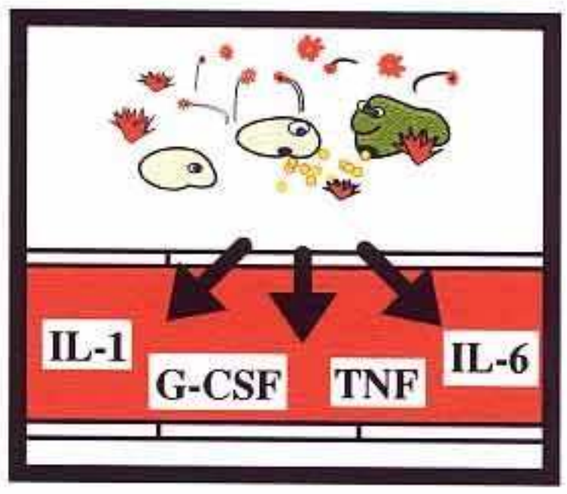
Although this T helper's 'hand' fits, if the macrophage doesn't release interleukin-1, the T helper cell cannot release any cytokines.

ERADICATING BACTERIAL INFECTIONS



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

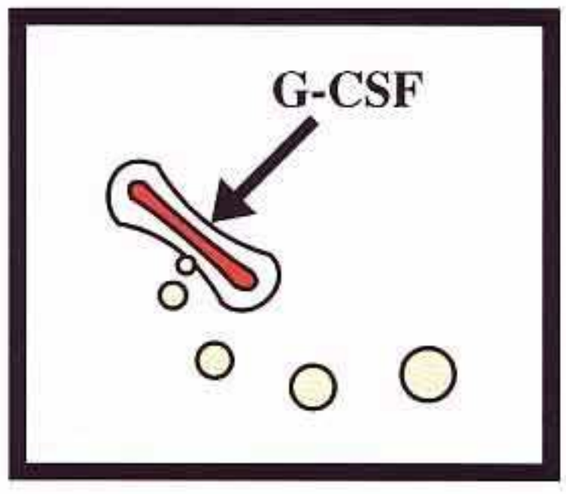
These immune cells will attempt to eliminate the invading microbes.



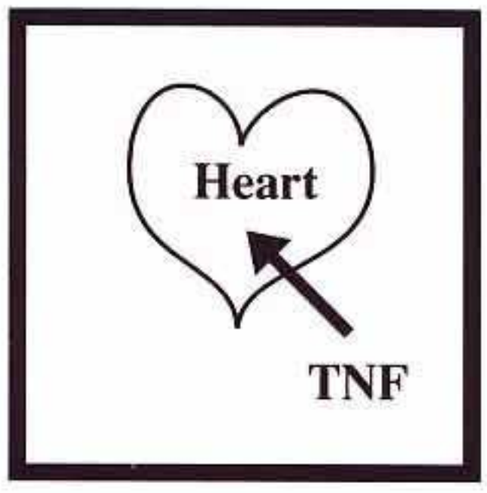
Cytokines released into the blood, will summon up extra help!!

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

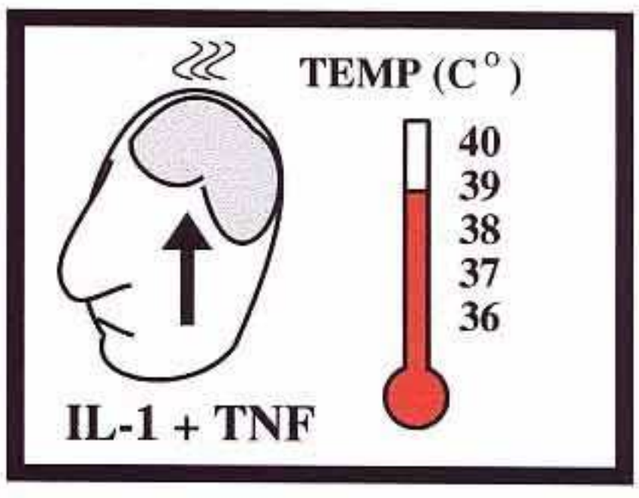
SYSTEMIC RESPONSES TO BACTERIAL INFECTIONS



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



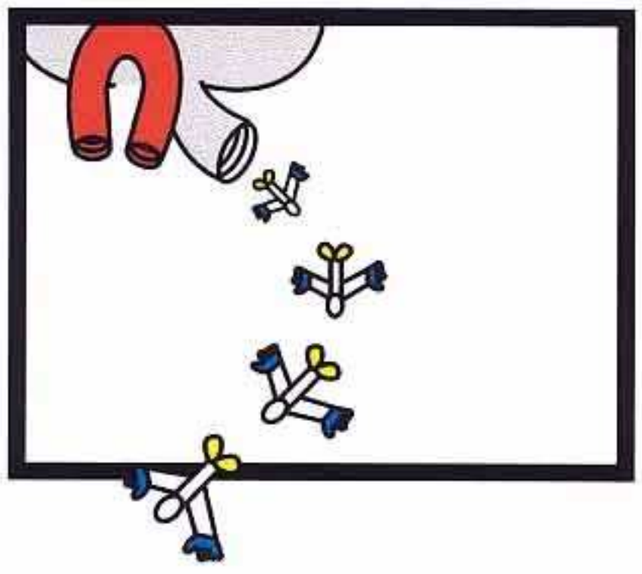
High levels of tumour necrosis factor, will affect heart rate.



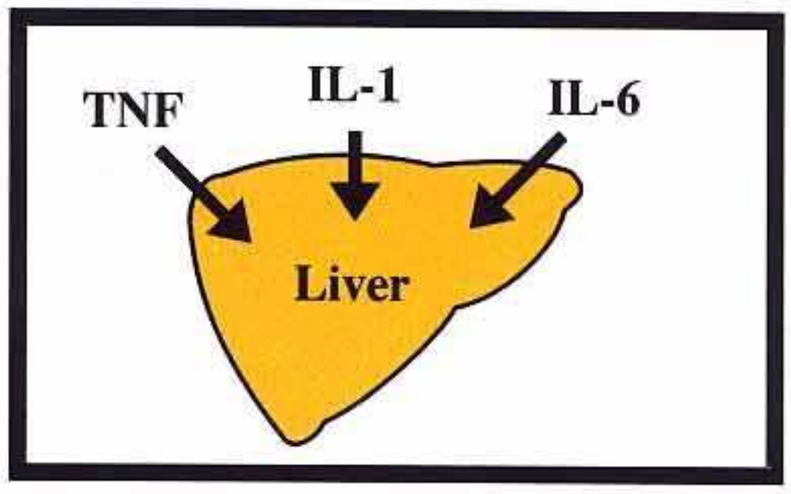
IL-1 and TNF triggers the hypothalamus into making prostaglandins, which will raise the body's temperature.

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.

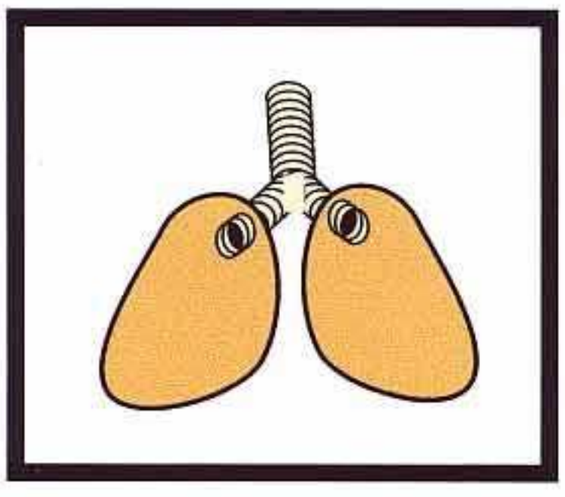
The liver releases decreased amounts of:-

Albumin

Transferrin

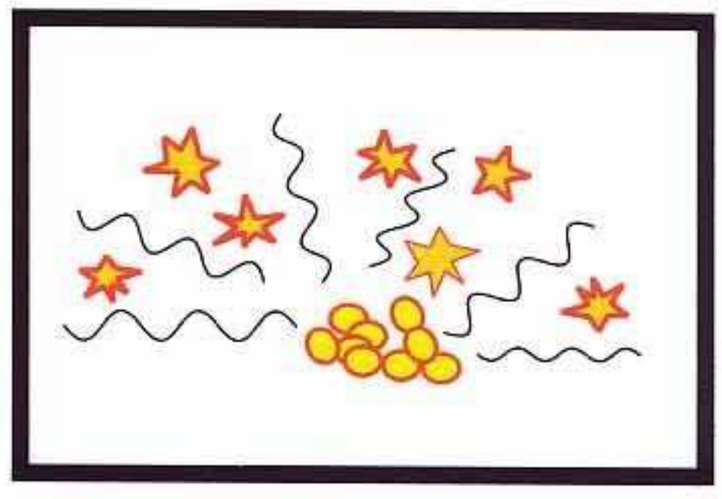
The decreased release of transferrin into the blood, deprives any replicating bacteria, of a ready supply of iron.

WHY IS INFECTED SPUTUM GREEN?

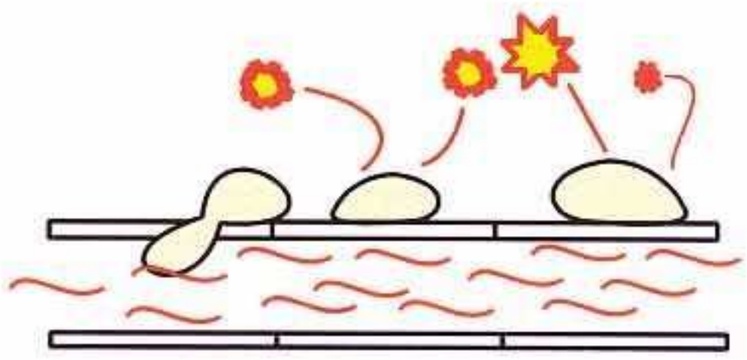


Normally our lungs only produce a small amount of watery mucus.

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



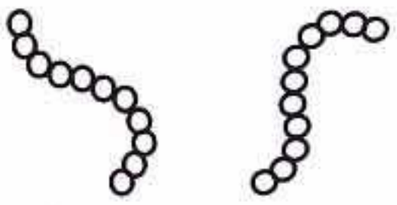
Inflammation released during a bacterial infection, stimulates excessive mucus production.



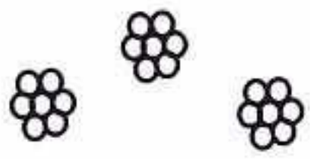
Neutrophils entering the lungs, use emzymes to kill the bacteria. Some of the enzymes contain copper and it is this which turns the mucus in the lungs green.

BACTERIAL CLASSIFICATION

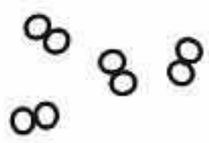
Round shaped bacteria



Streptococcus
(grow in chains)



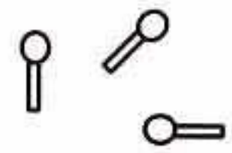
Staphylococcus
(grow in bunches)



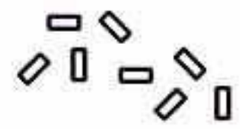
Diplococcus
(grow in pairs)

Rod shaped bacteria

Spore forming
aerobic bacillus

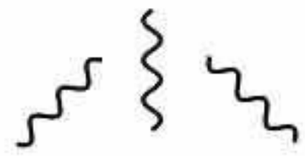


Spore forming
anaerobic bacillus

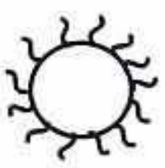


Non spore
forming bacillus

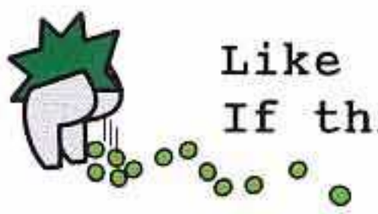
Helicoidal bacteria



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.

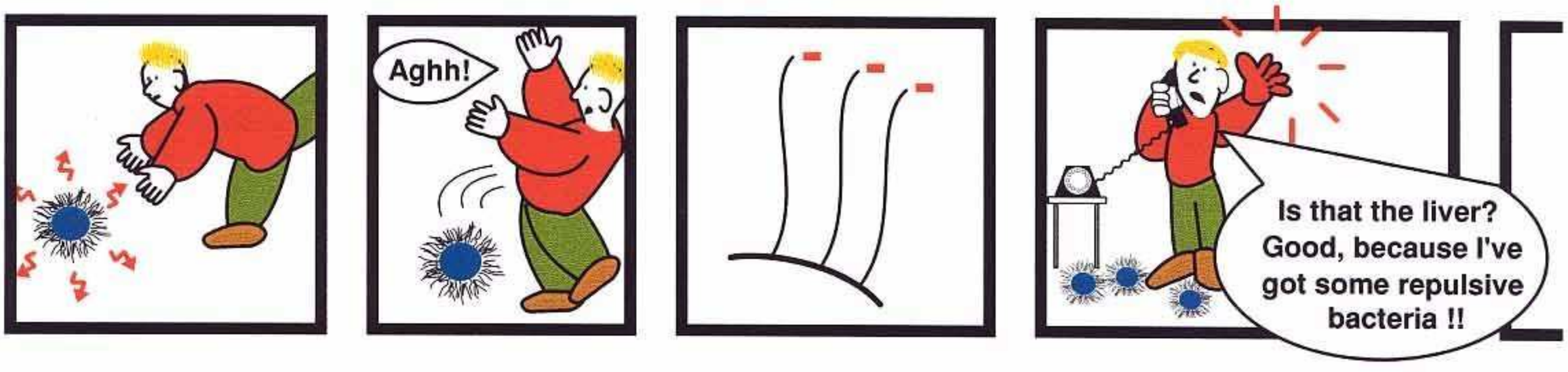


Like all living things, bacteria produce waste. If this then causes disease, it is called "exotoxins".

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

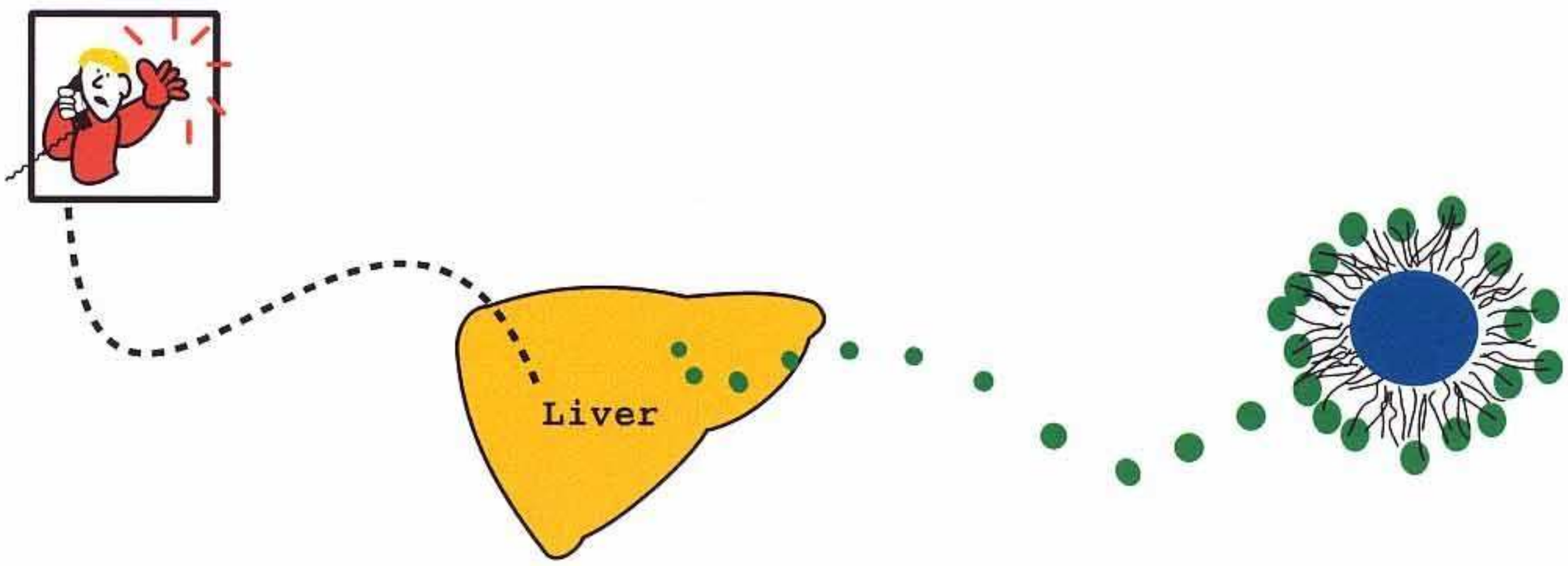
This bacteria is covered in M proteins, giving it an unusual 'hairy' appearance.



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

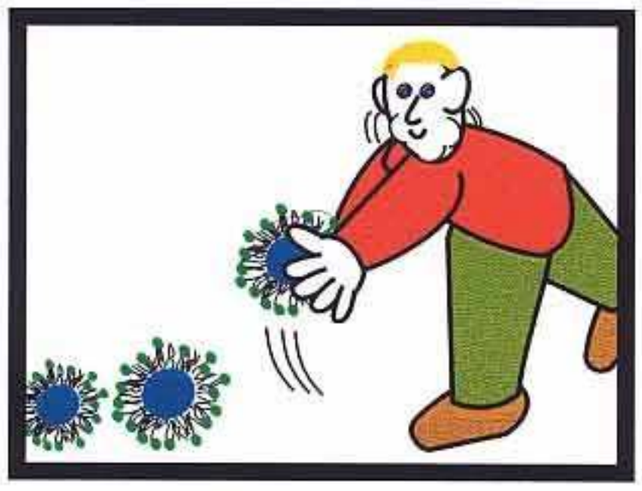
A negative charge is found at the tips of the 'hairs'.

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

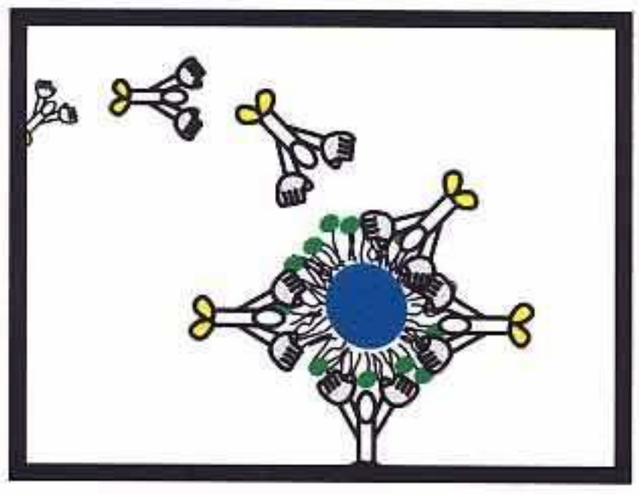


When macrophages encounter this type of bacteria, they release factors which are carried by the blood to the liver.

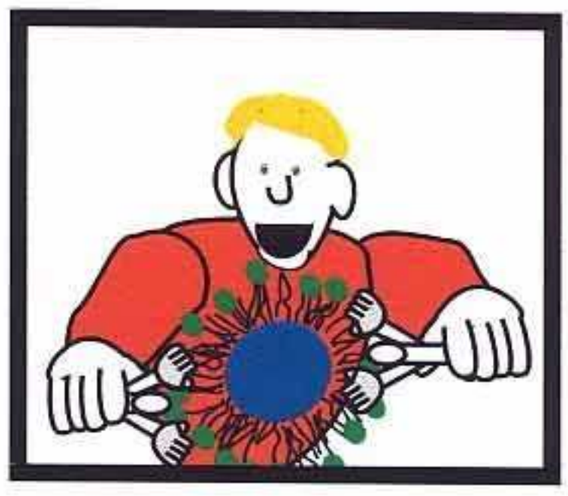
The liver responds by releasing opsonins, which attach onto the ends of the M proteins and neutralise its negative charge.



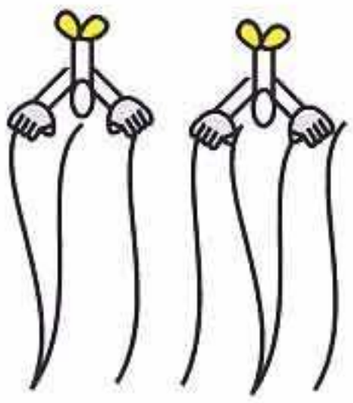
Once coated in opsonins, the 'hairy' bacteria can now be picked up and 'eaten'.

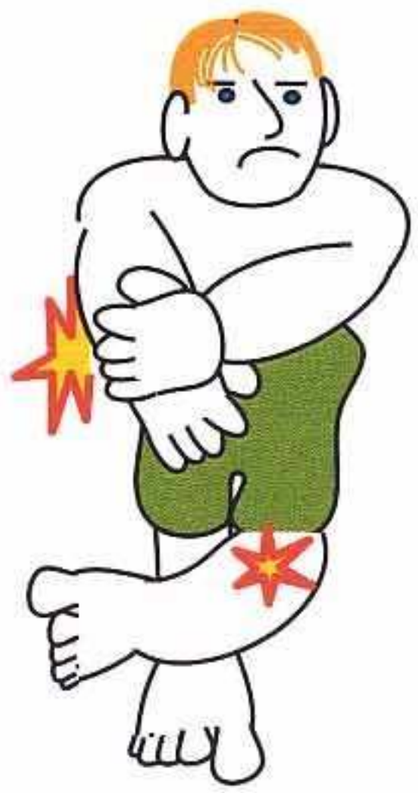


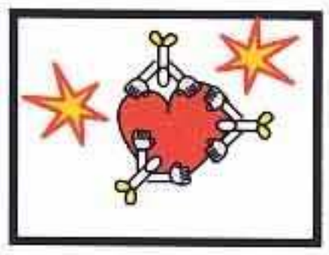
It is not long before IgG start arriving and they too, latch onto the M proteins.

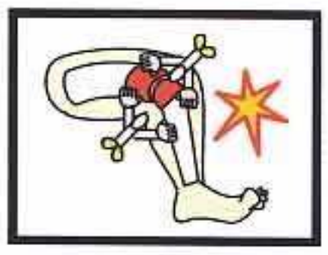


These help to make his job even easier!!!





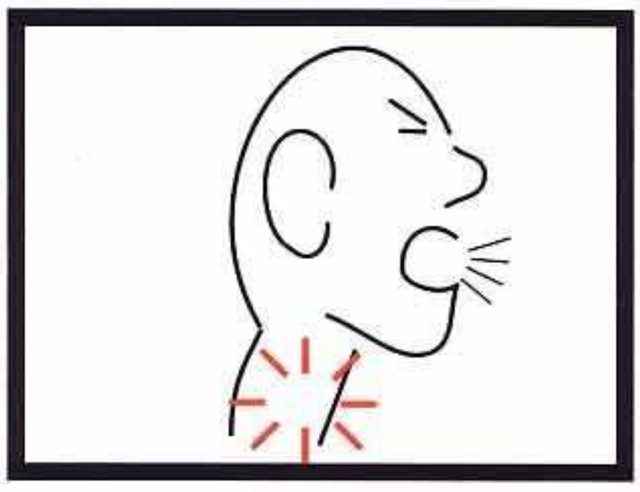




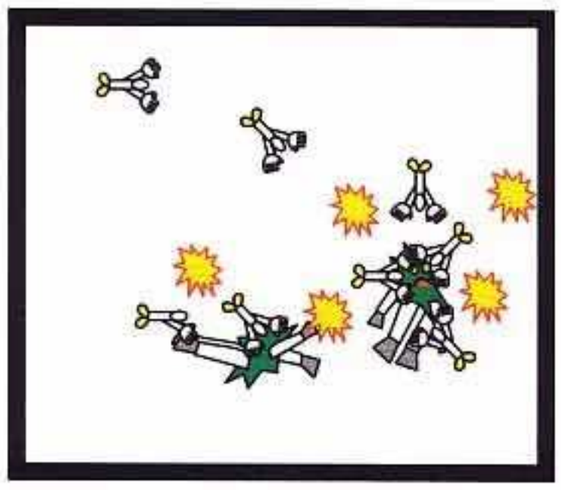
Unfortunately for some children, these antibodies not only 'grab' the M proteins, but they also attach onto the child's joints and heart muscle. This can be life threatening (see page 62).

ACUTE GLOMERULONEPHRITIS

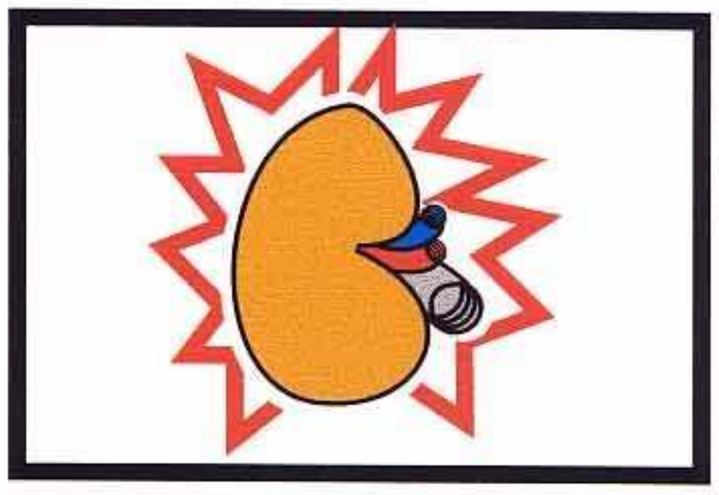
This condition can occur, following a haemolytic streptococcal bacterial infection, somewhere in the body.



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

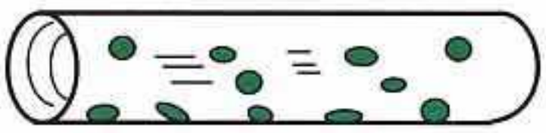


After a couple of weeks, antibodies appear and eliminate the bacteria.

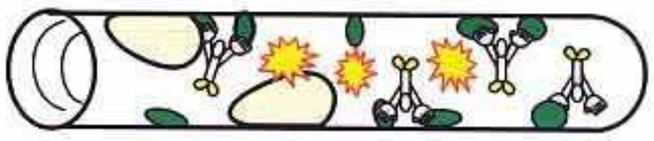


But as his sore throat improves, Ivor starts having excruciating kidney pains.

SO WHAT WENT WRONG?

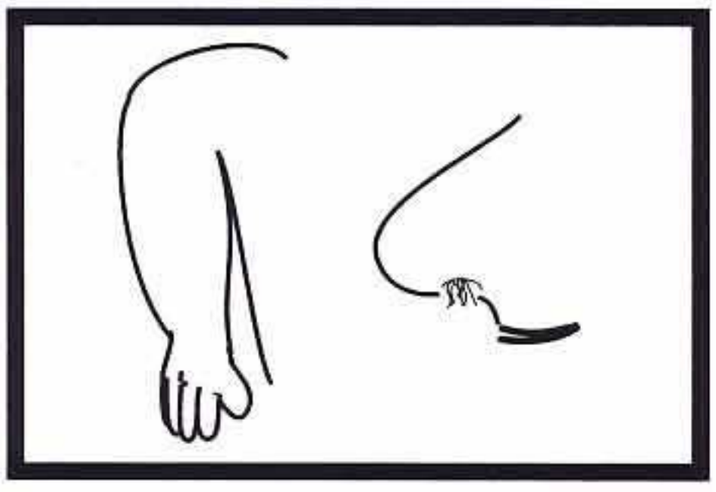


When the sore throat began, pieces of the bacteria became attached to the walls of the glomeruli inside the kidneys.

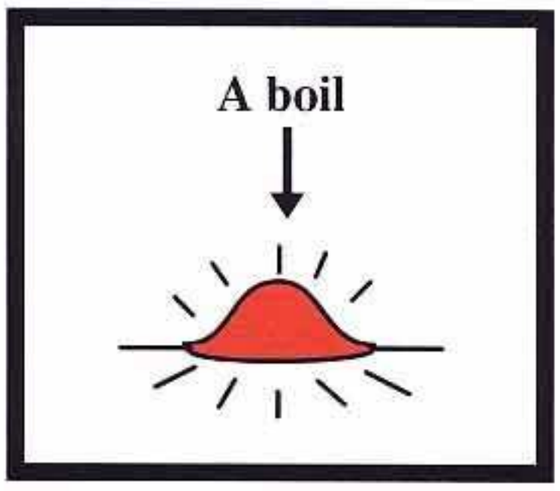


2 weeks later, antibodies attach onto the bits of microbe in the kidneys, activating complement and neutrophils.

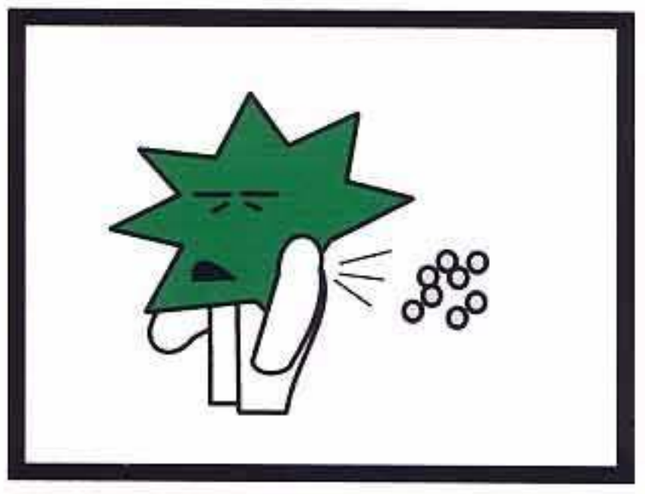
STAPHYLOCOCCAL BACTERIA



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



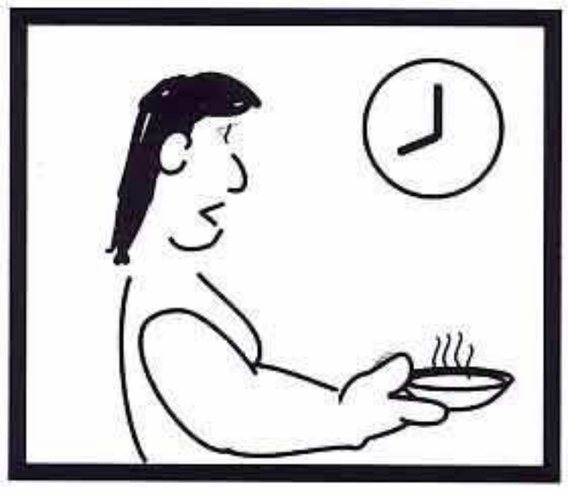
But if they get under the skin, a superfical infection like a boil can develop.



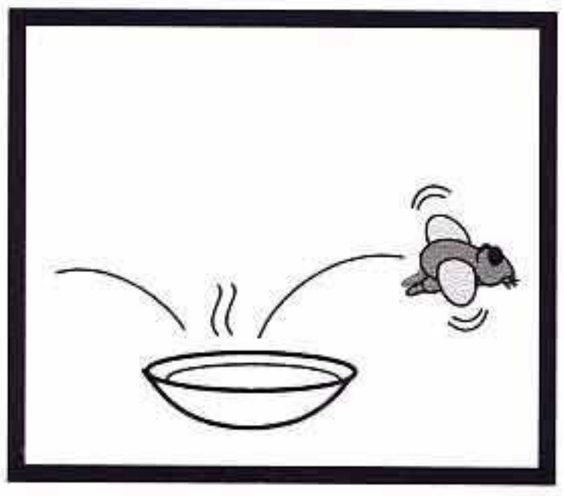
Certain strains of staphylococcal bacteria, release nasty waste products (toxins).

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.

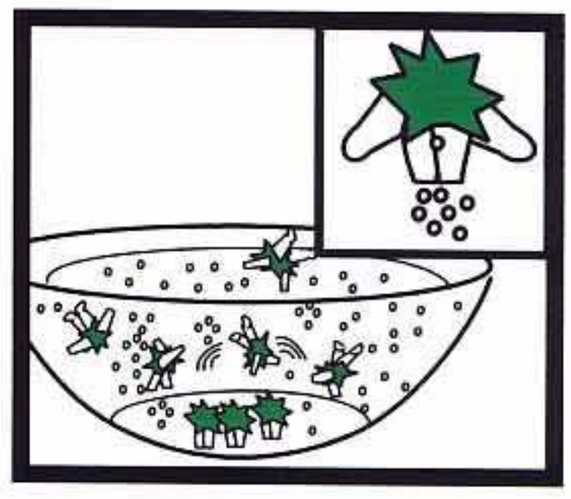
FOOD POISONING



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

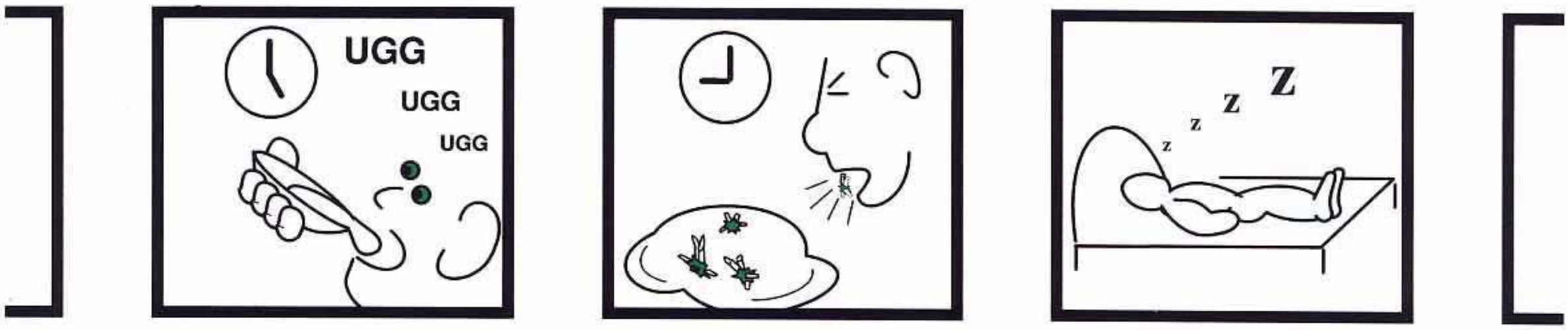


Unfortunately, while she is out of the room, it becomes contaminated.



Staphylococcal bacteria start to replicate and release enterotoxins.

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



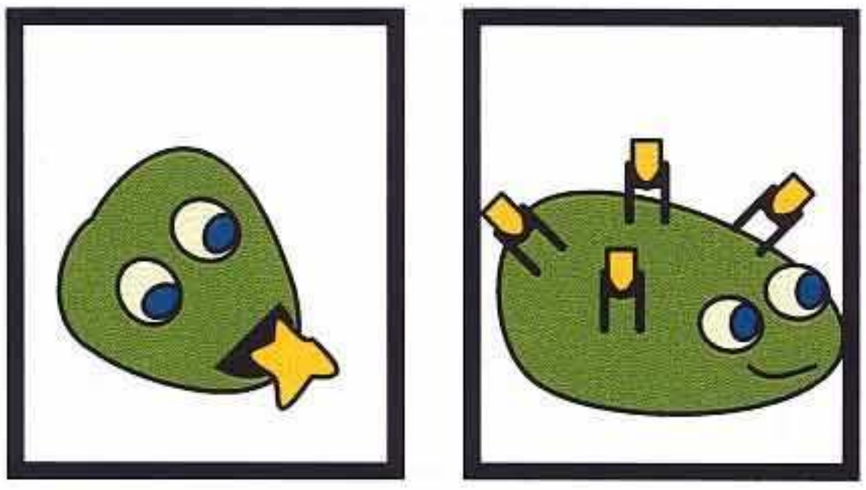
Sometime later, Simon returns home and gulps down the soup.

That evening he is sick.

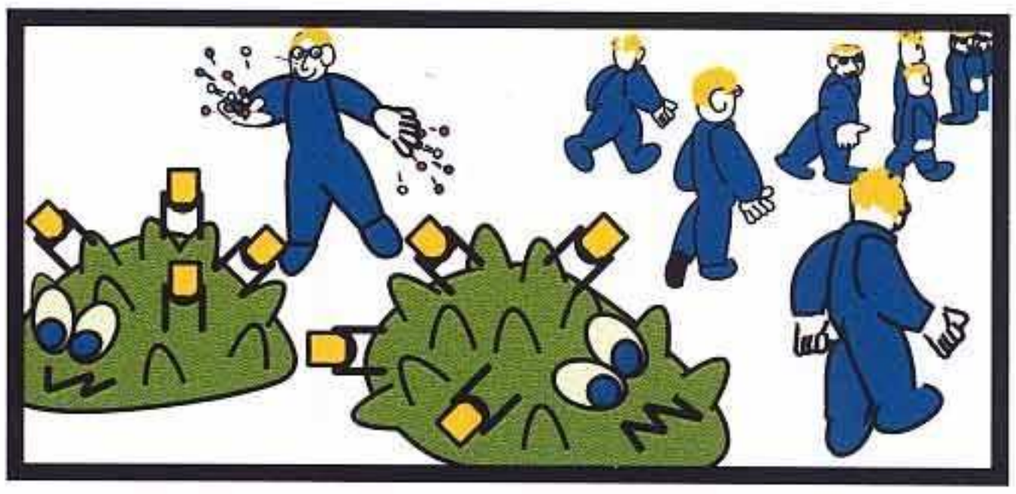
But once the toxins have been expelled, things can then get back to normal.

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

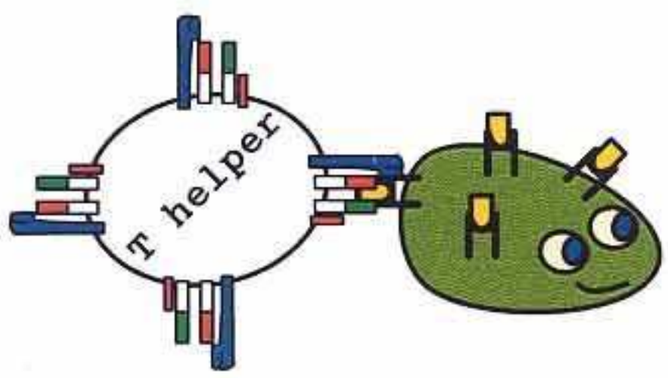
THE NORMAL IMMUNE RESPONSE TO WASTE REMOVAL

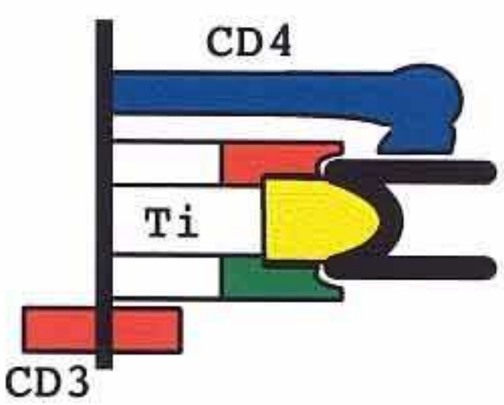


After 'eating' waste material, small pieces are normally expressed, attached to 'attack' proteins.



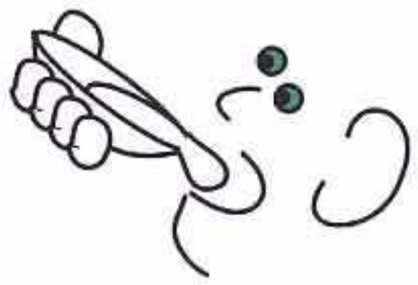
Although many T helper cells then want to help, most of them have the wrong shaped 'hand' and are disappointed!

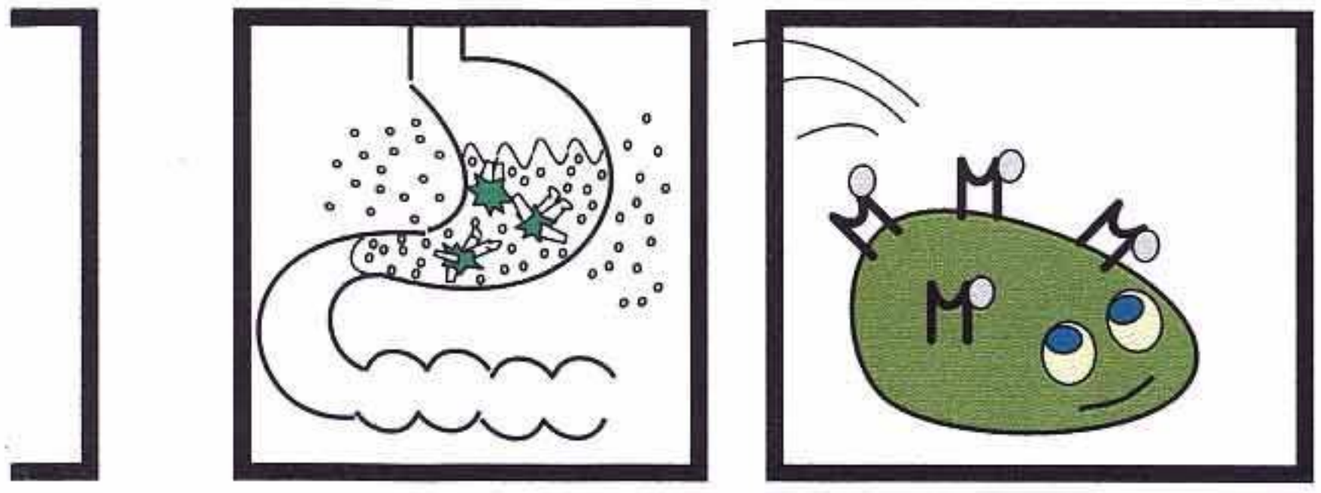




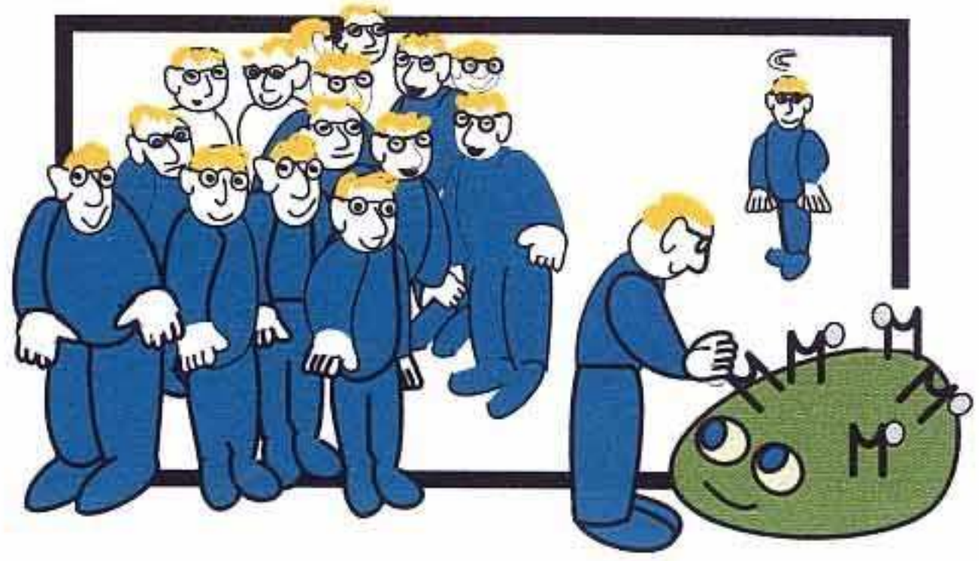
Normally, the T helper's Ti shape (see page 85), is all important.

SO WHY IS CONTAMINATED FOOD EJECTED SO QUICKLY?



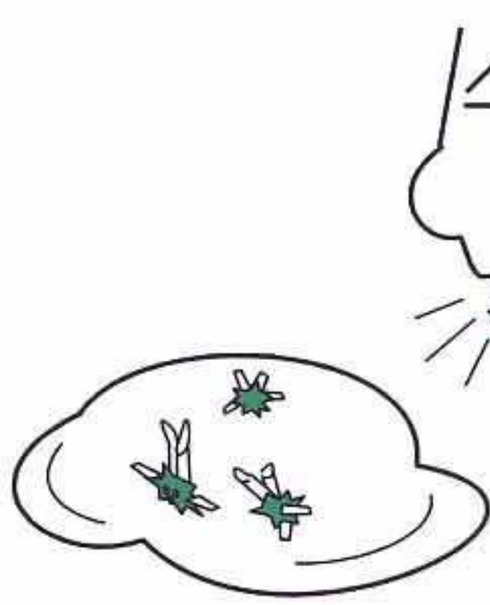


Enterotoxins enter the stomach and rapidly diffuse into the tissues. They then attach onto the outside of the 'attack' proteins, without first being 'eaten'.



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

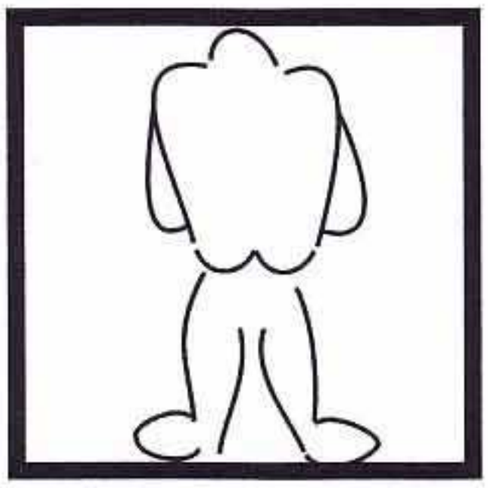
An excessive T helper response follows and this leads to many more macrophages than normal being galvinised into action.



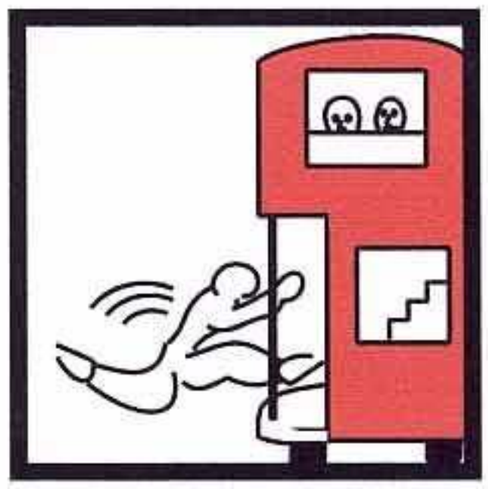
The resulting rapid build up of factors from the macrophages now causes the stomach to violently expel the contaminated food.

TOXIC SHOCK SYNDROME

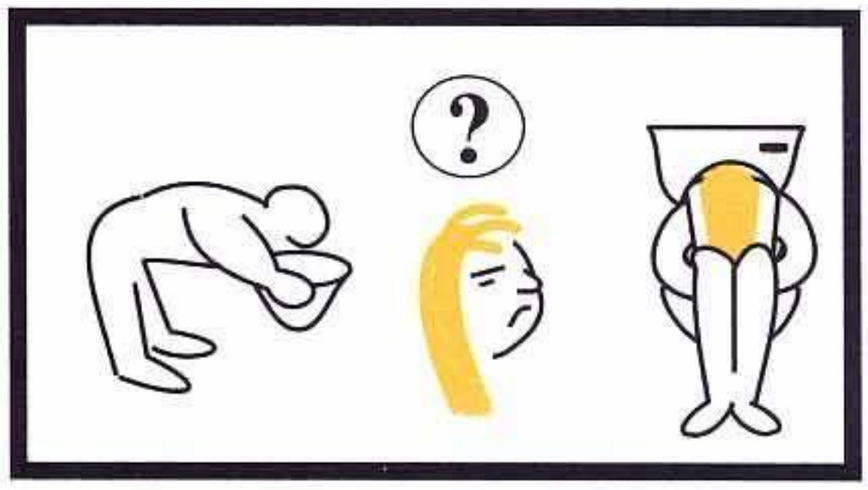
A potentially lethal condition.



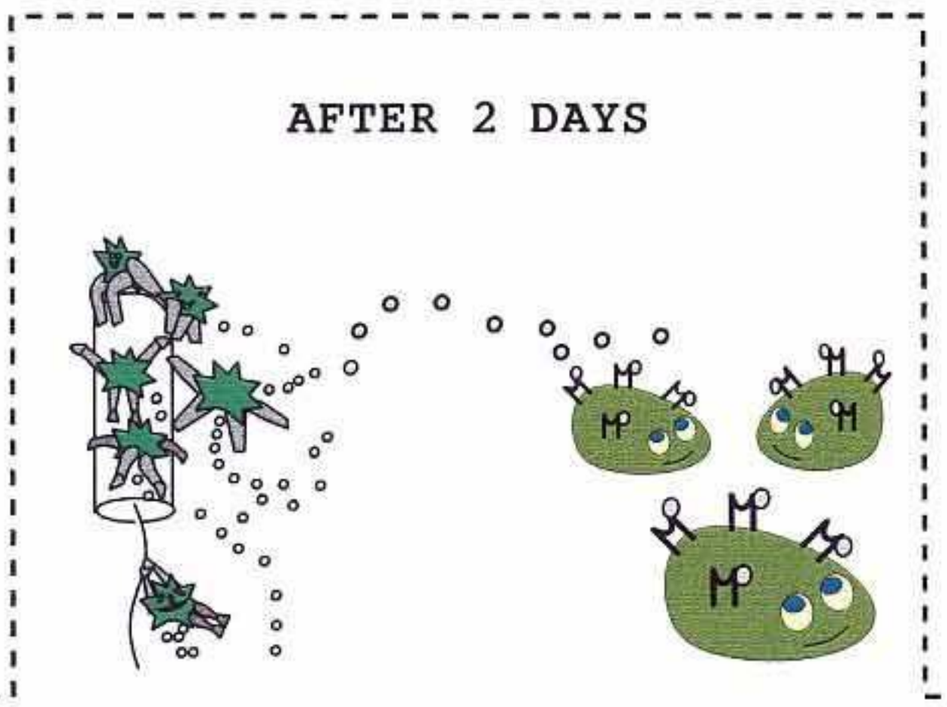
This morning, Beccy realises she is going to need a tampon.



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



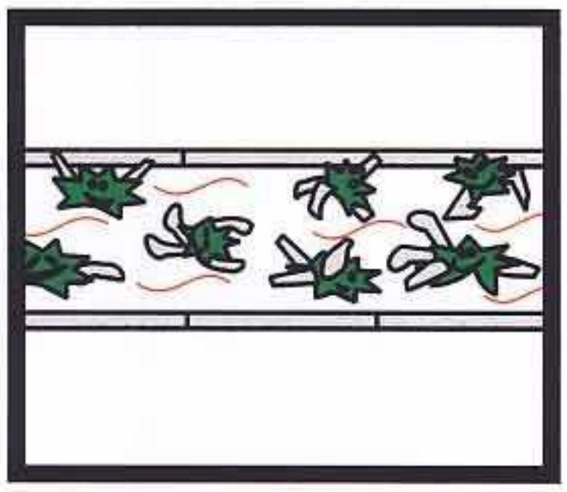
Several days later and Beccy starts to experience flu-like symptoms and memory loss.



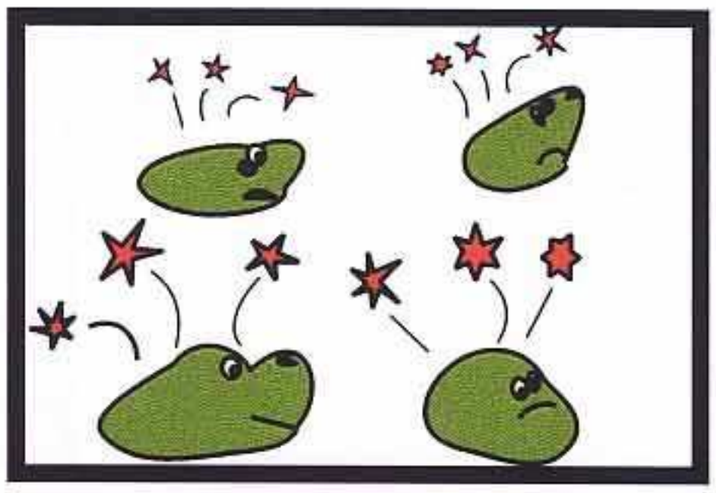
Staphylococcal bacteria living on her tampon, are releasing toxins, which attach directly onto the 'attack' proteins.

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

SEPTIC SHOCK



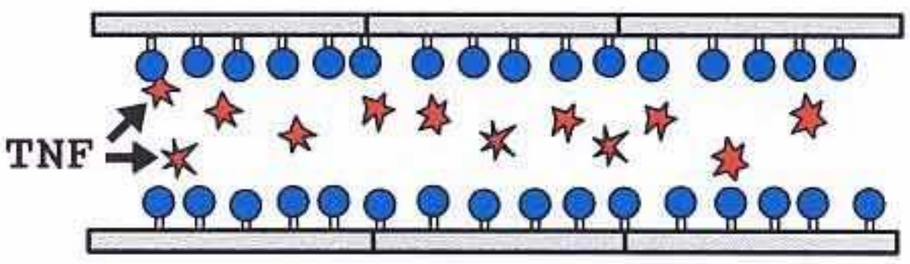
These gram - negative bacteria have infected someone's blood.



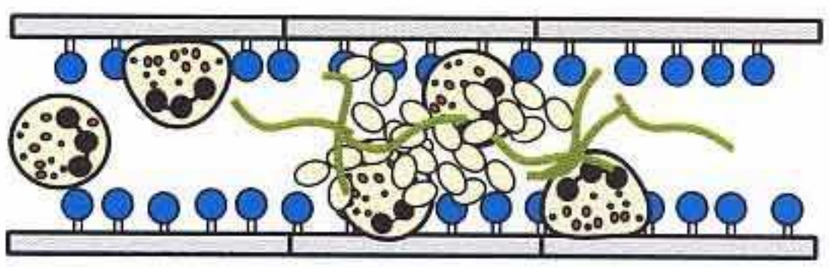
Endotoxins from the bacteria, then trigger macrophages into releasing tumour necrosis factor.

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.



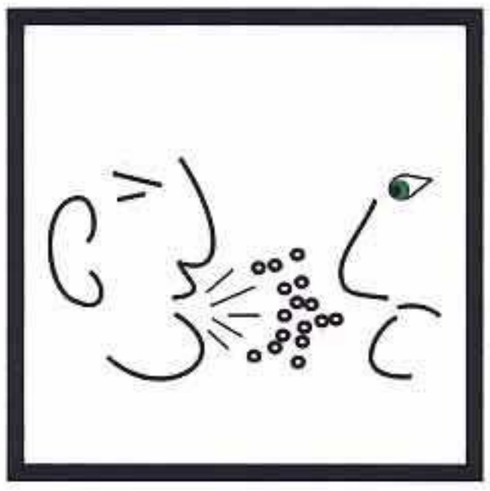
High levels of TNF also cause endothelial cells lining the blood vessels to express surface markers.



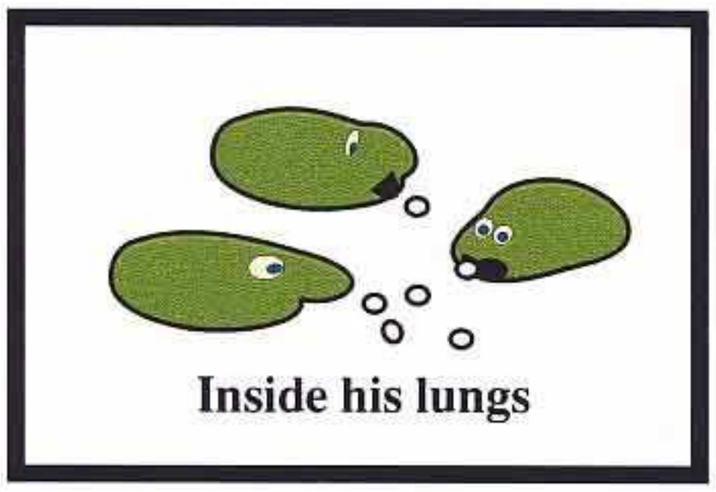
Platelets, neutrophils and fibrin now attach onto the surface markers and could block small blood vessels.

MYCOBACTERIUM TUBERCULOSIS (TB)

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



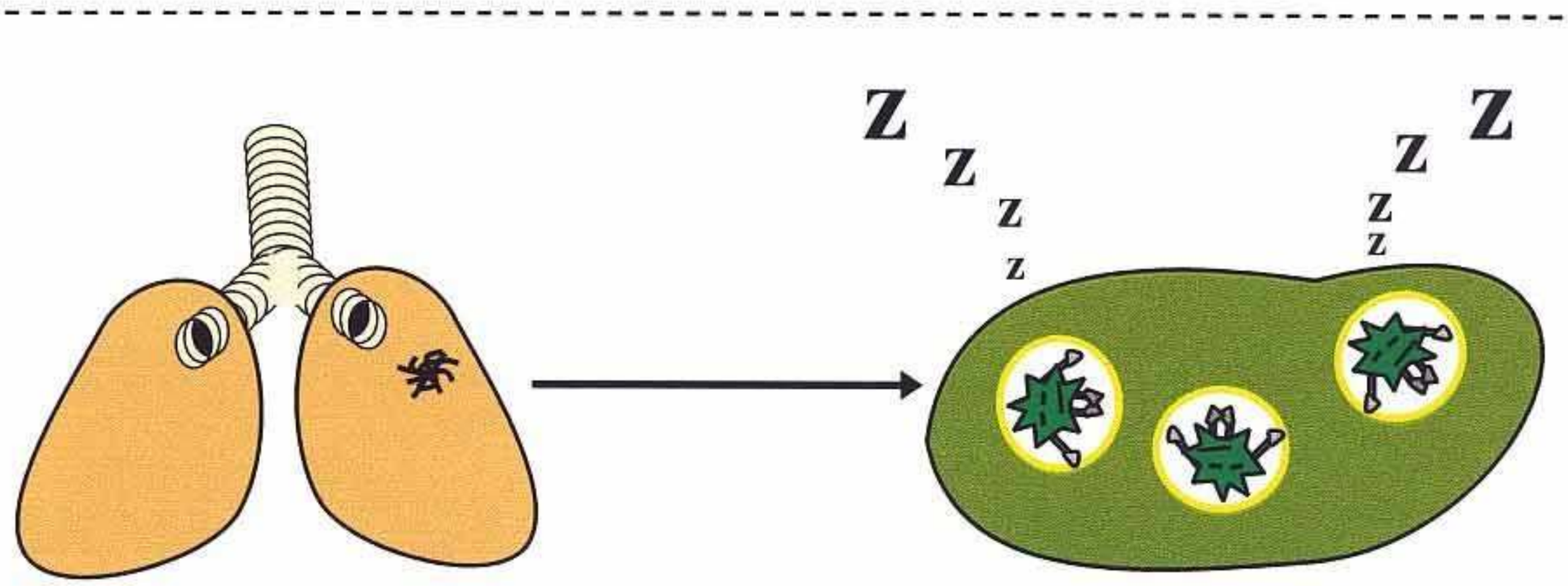
Infected droplets are inhaled from someone with active TB.



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.

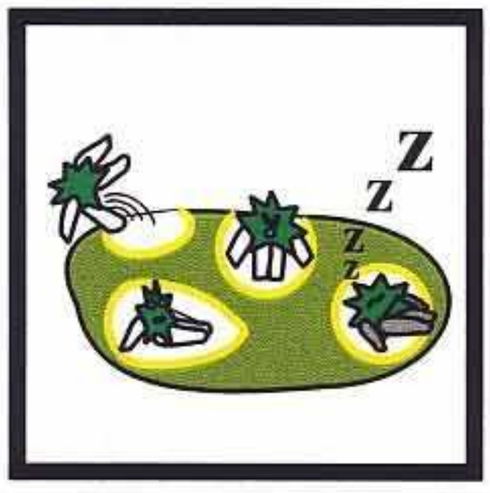
So without sufficient T helper stimulation, the bacilli can survive inside the macrophage.



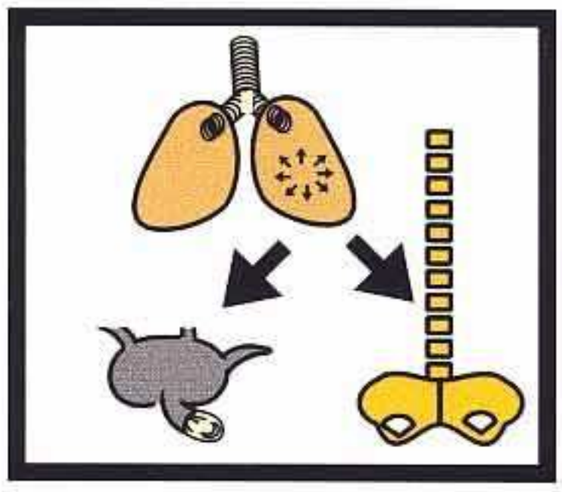
A calcified lesion may appear, following the primary infection.

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

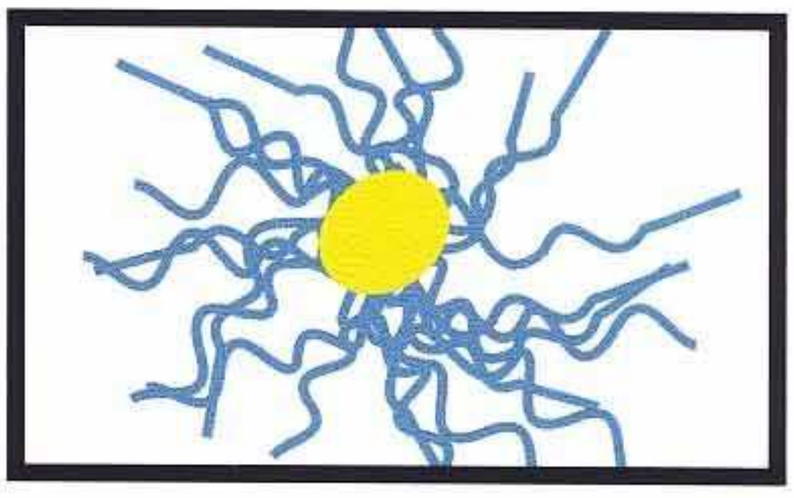
MONTHS LATER AND A PERIOD OF ILL HEALTH



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



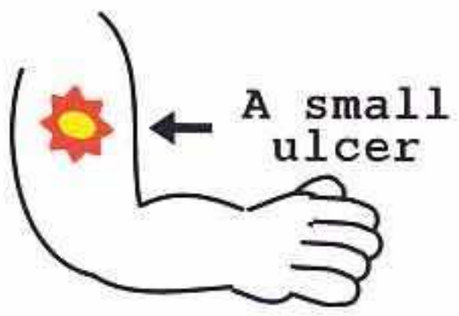
Soon tuberculosis lesions start to appear at other sites in the body.



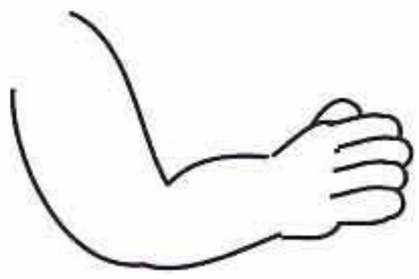
A typical tuberculosis lesion has a 'cheesy' centre and surrounding fibrous tissue, containing activated macrophages and T helper cells.

THE HEAF TEST SHOWS IF YOU ARE PROTECTED AGAINST TUBERCULOSIS

Killed tuberculosis bacilli are injected.



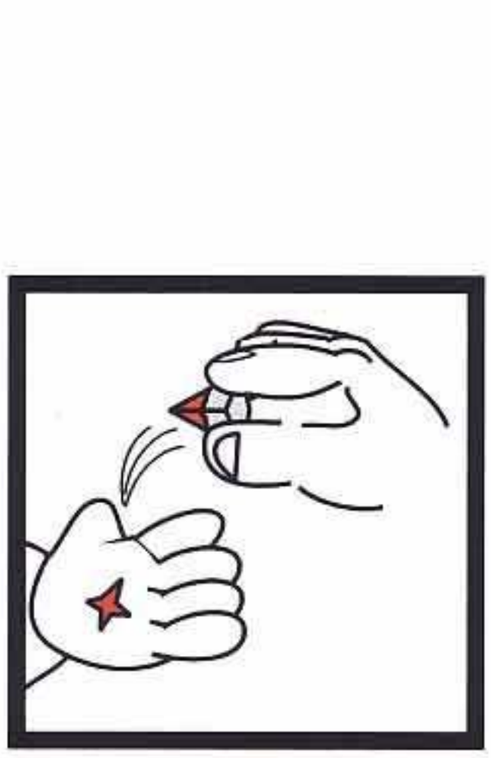
A good / positive tuberculin reaction.



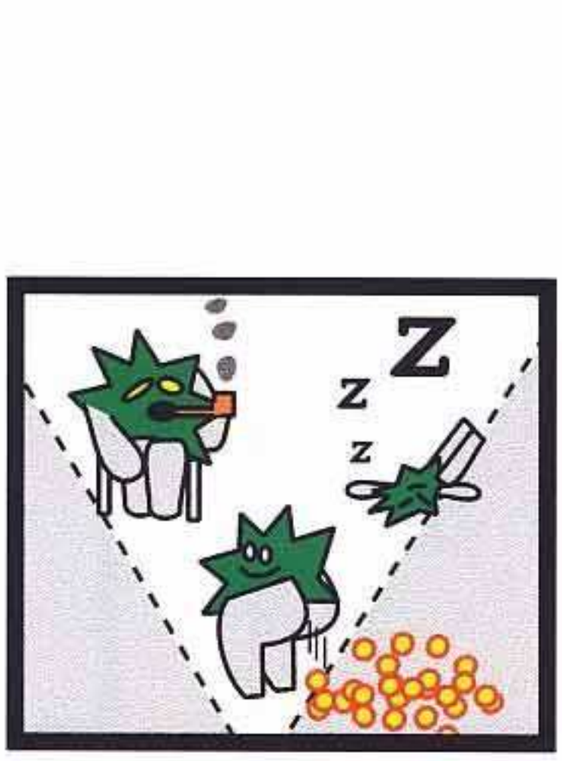
A bad / negative tuberculin reaction.

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

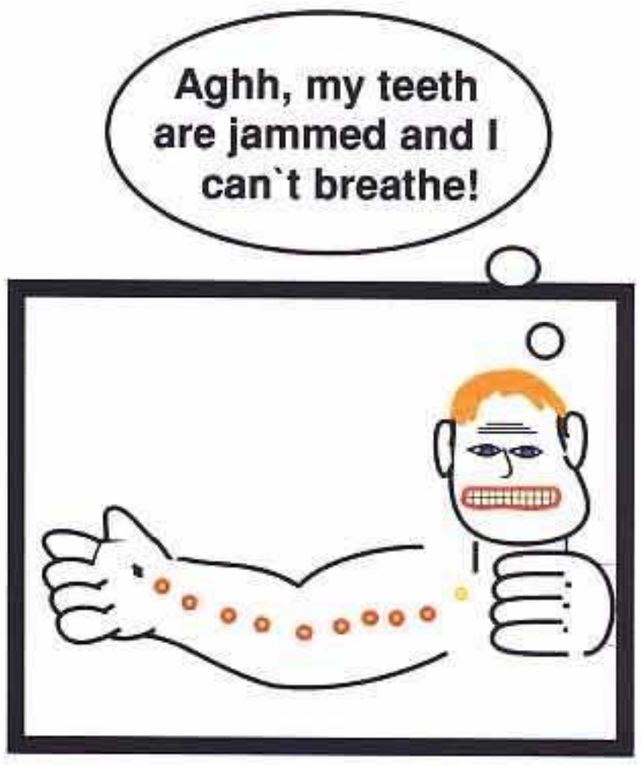
TETANUS



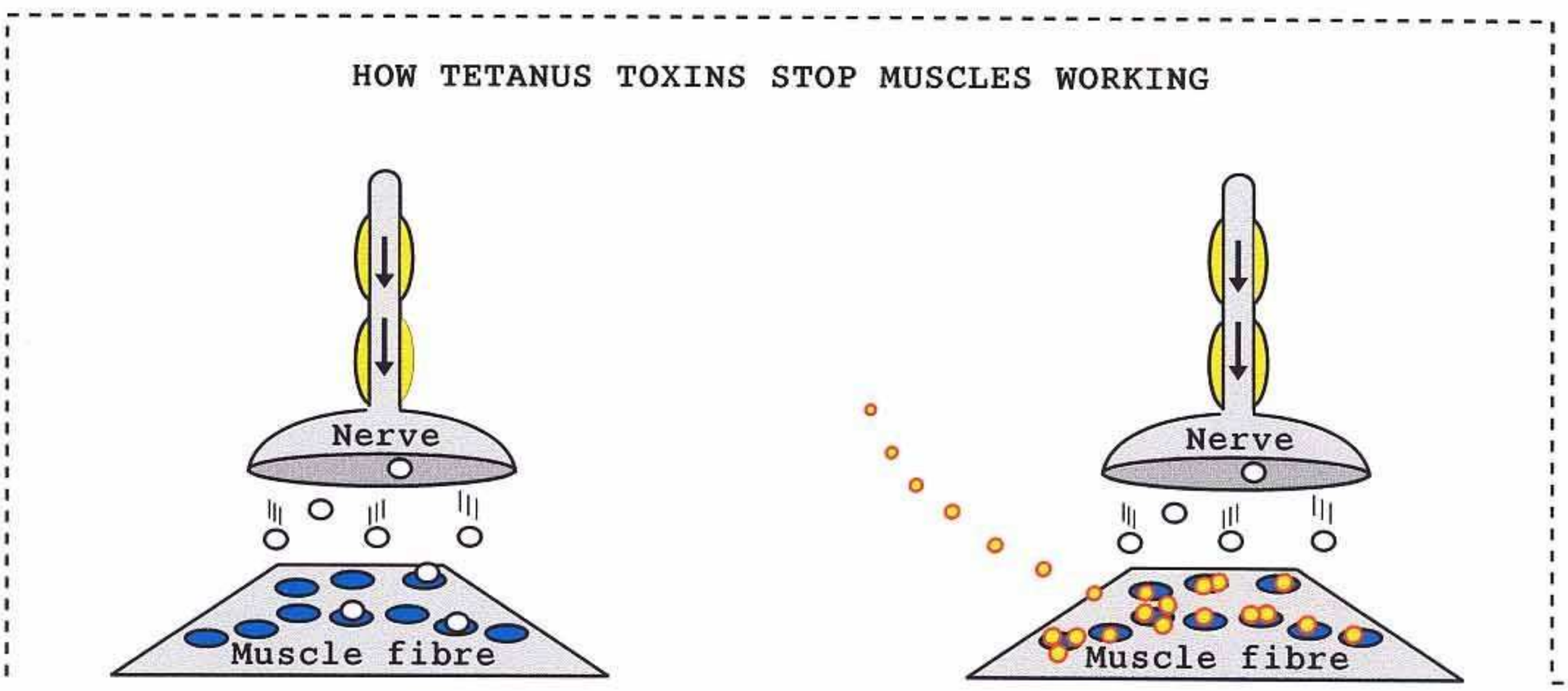
Just another garden injury, or is it?



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



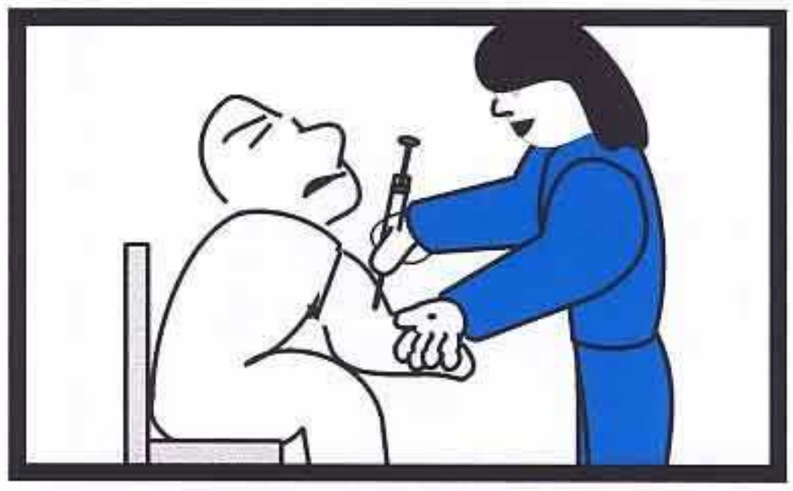
Soon they start to release waste (exotoxins), which could be fatal!!!



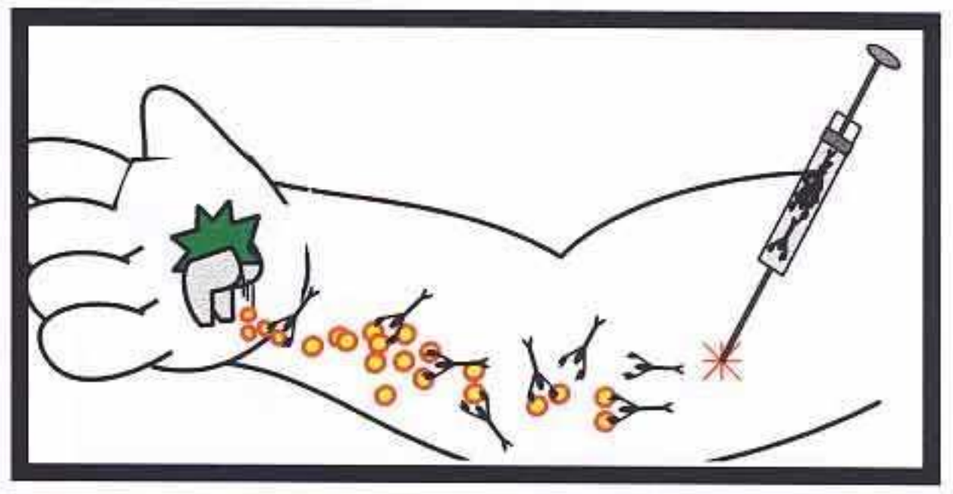
Normally, nerve impulses reaching the end of a nerve, trigger acetylcholine to be released onto a muscle, causing it to contract.

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

A TEMPORARY SOLUTION

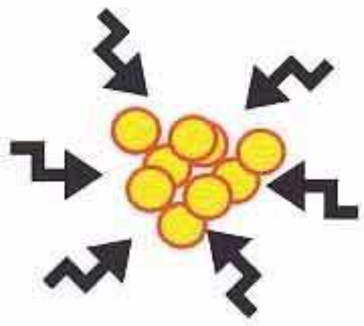


The nurse injects antibodies with 'hands', that fit the tetanus toxins.

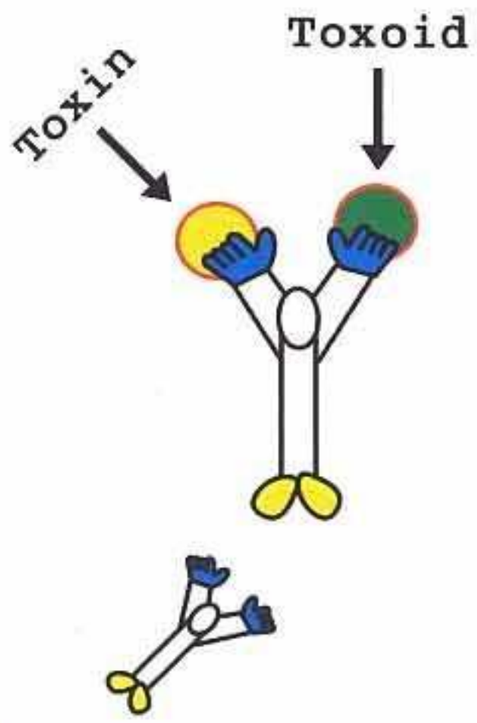


They 'grab' the toxins, but as these antibodies are not made by the patient, they will soon disappear.

THE PERMANENT SOLUTION



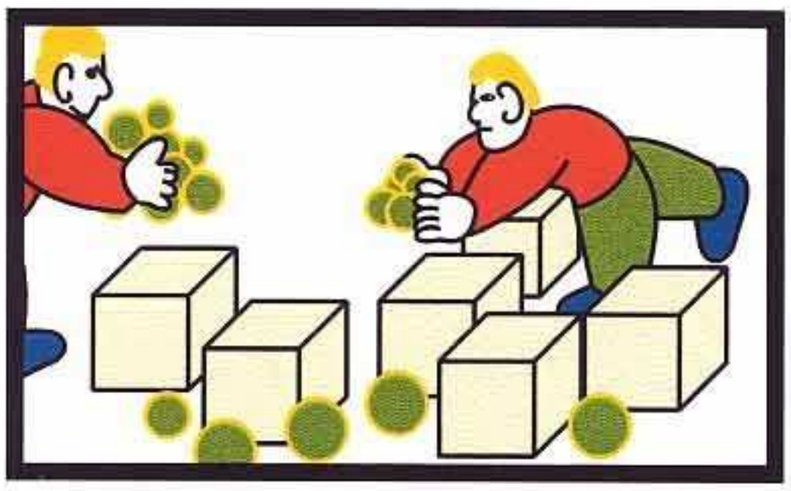
Tetanus toxins are treated so that they become harmless, but their shape is unaltered.



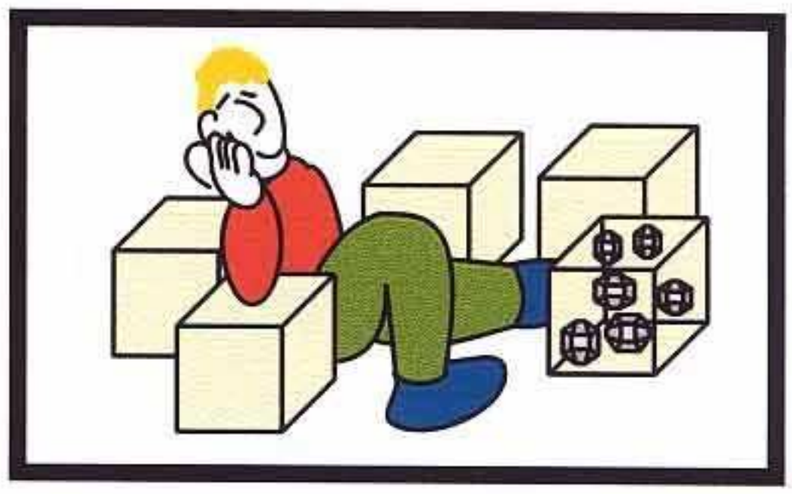
The harmless toxins, now called "tetanus toxoid", is injected.

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!