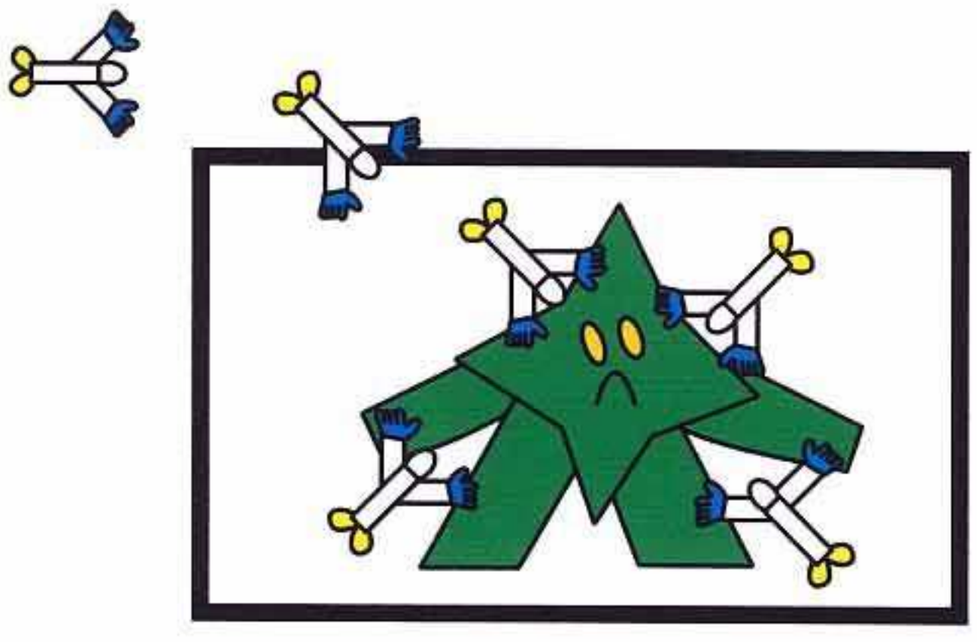
CHAPTER TWO

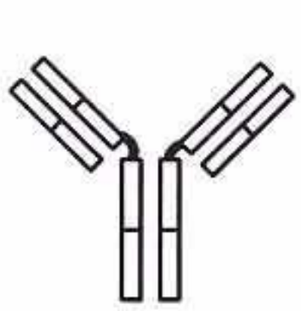
ANTIBODIES

ANTIBODIES ARE USED TO APPREHEND INVADING MICROBES

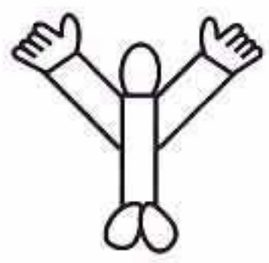


Easy reading

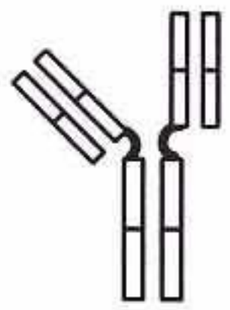
Technical information

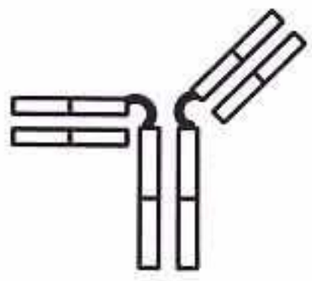


Antibodies are 4 chains of molecules linked together.



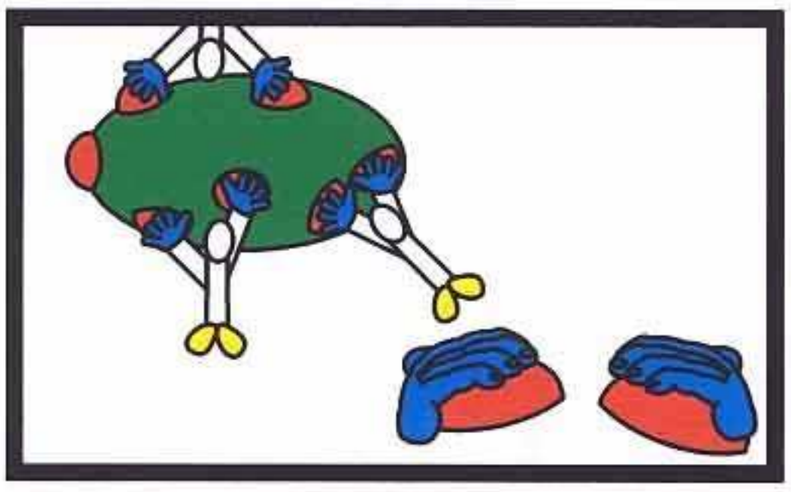
These function as 'hands', 'arms', a 'body' and 'feet'.

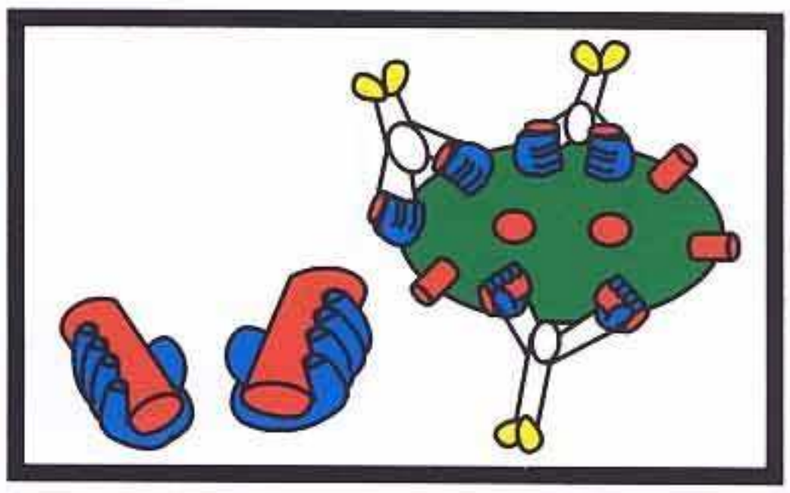




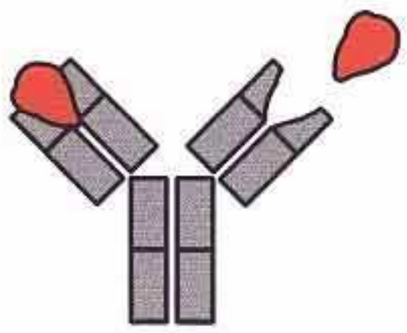
The 'arms' are hinged so that they can move.

'HANDS'



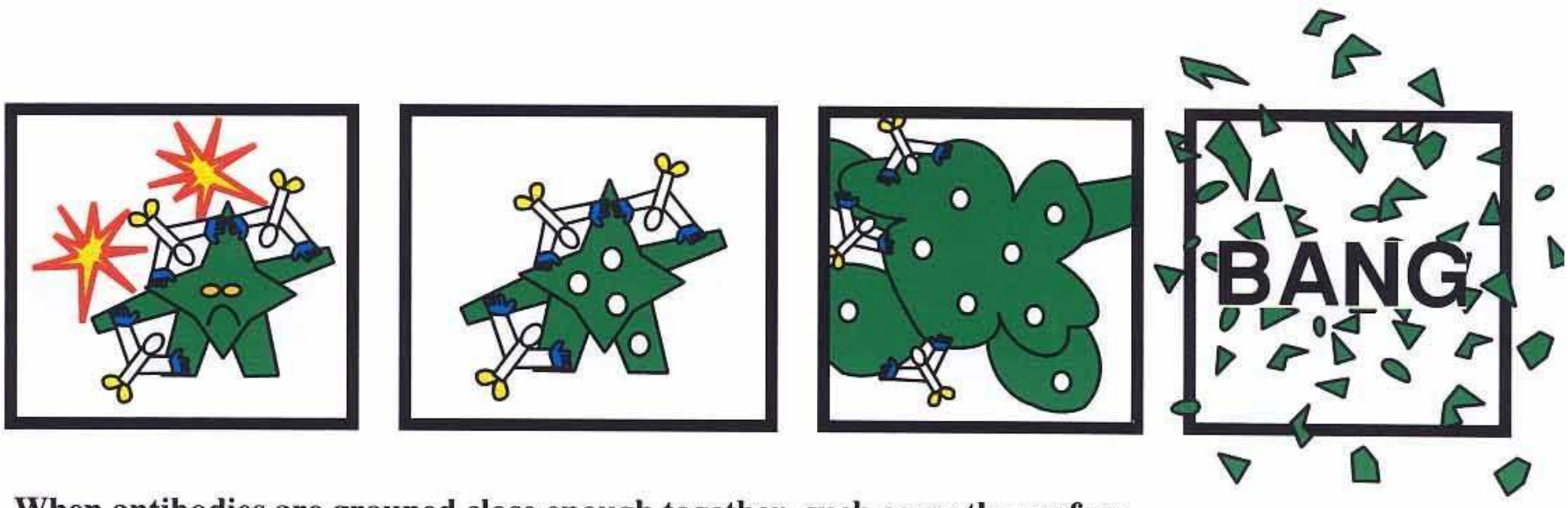


Both these sets of antibodies are identical, apart from the shape of their 'hands'.

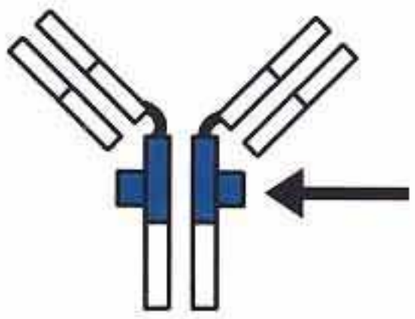


As an antibody's 'hand' shape is fixed, to apprehend a microbe, the 'hands' must fit snugly around and over the target.

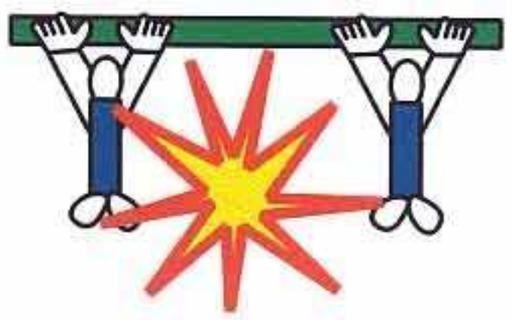
THE 'UPPER BODY'



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

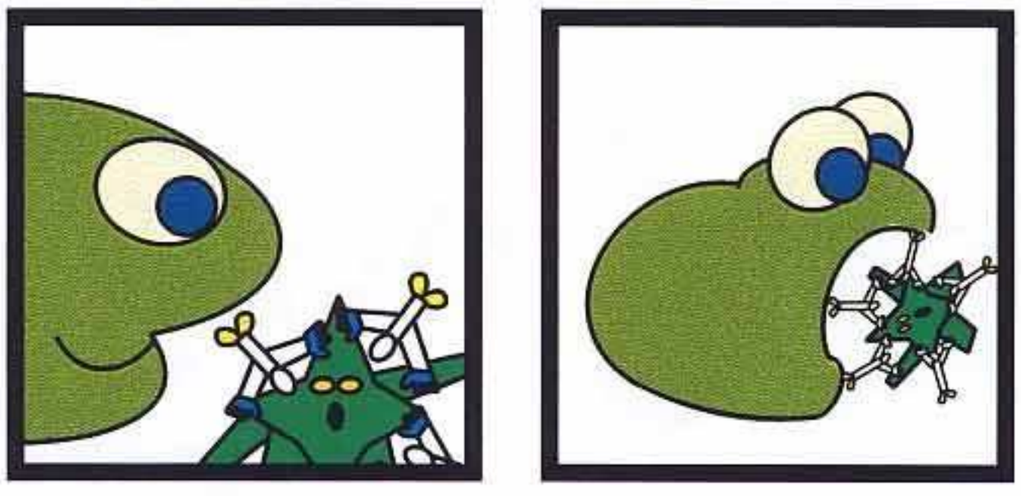


Complement activators are located on the antibody's upper 'body'.

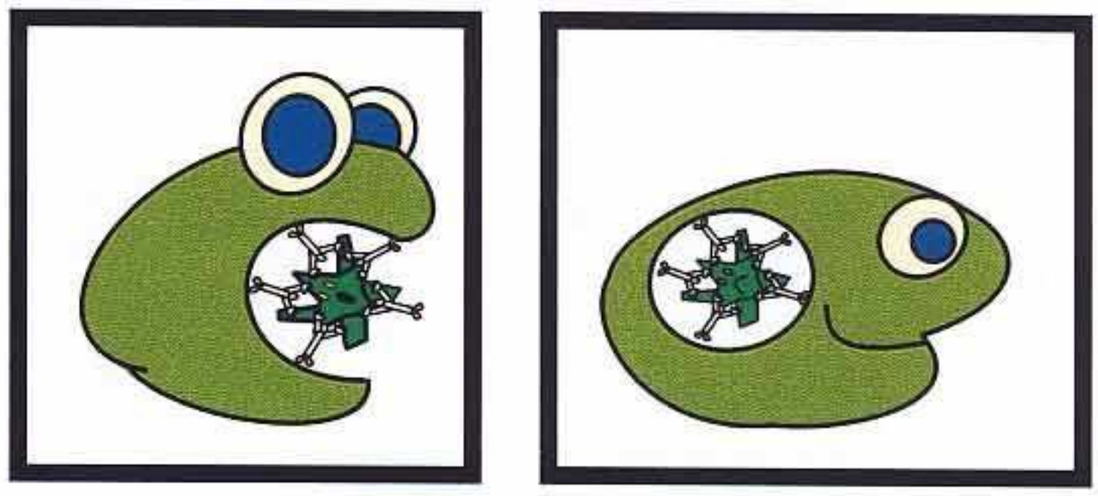


But to detonate complement, 2 antibodies must attach very close together.

THE 'FEET' / LOWER BODY

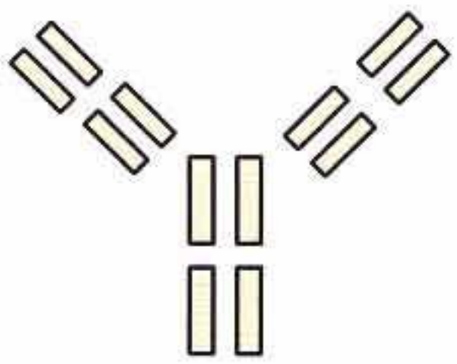


Macrophages and neutrophils, use surface receptors to attach onto the 'feet' of those antibodies coating the surface of a microbe.

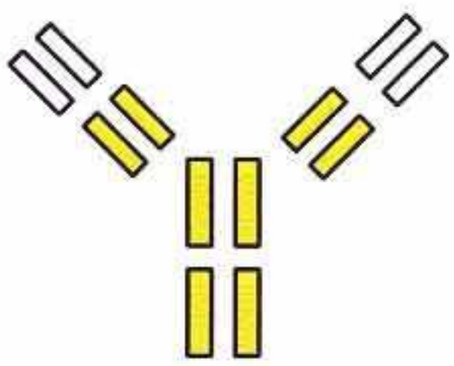


As they attach onto more and more antibodies, so the microbe is drawn inside the immune cell (like a zip being fastened), until it is totally enclosed.

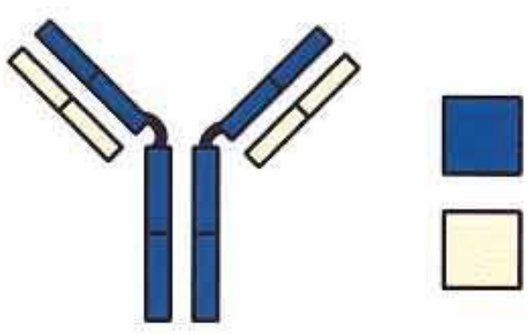
The 'feet' (end section) of the antibody are used by immune cells, to attach (opsonize) onto foreign material.



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

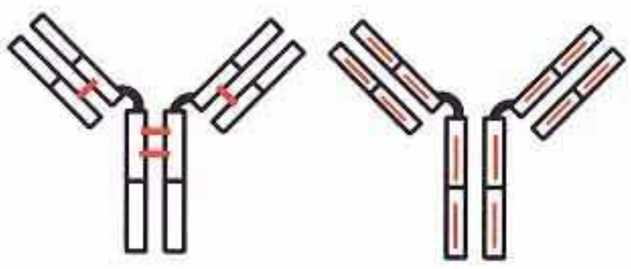


The constant domains (shown in yellow) are of a universal design.

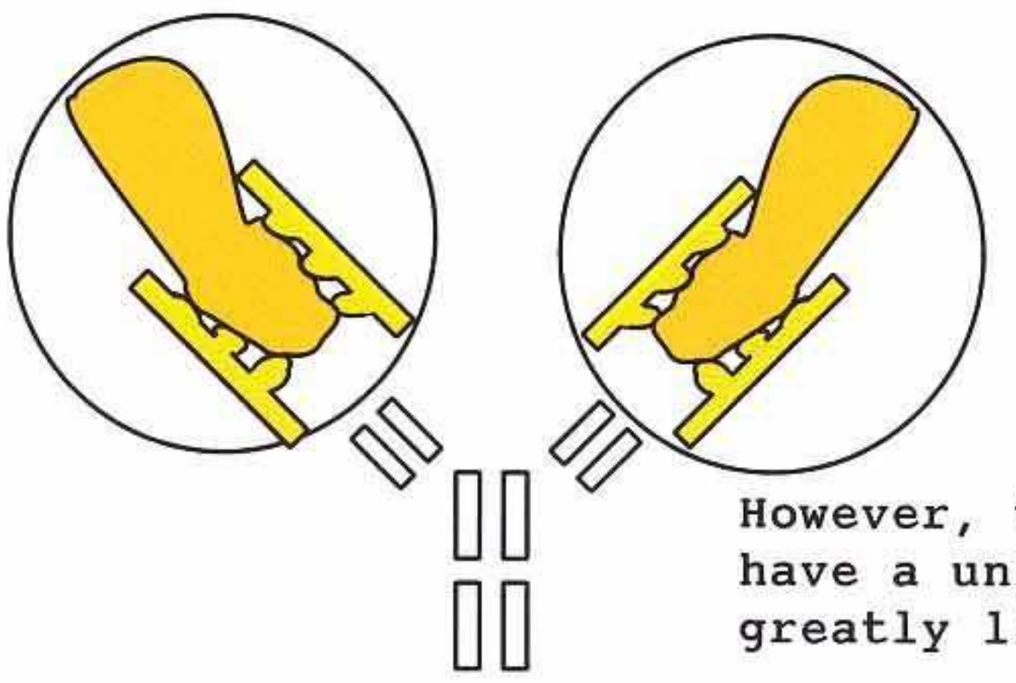


2 heavy (long) molecular chains.

2 light (short) molecular chains.

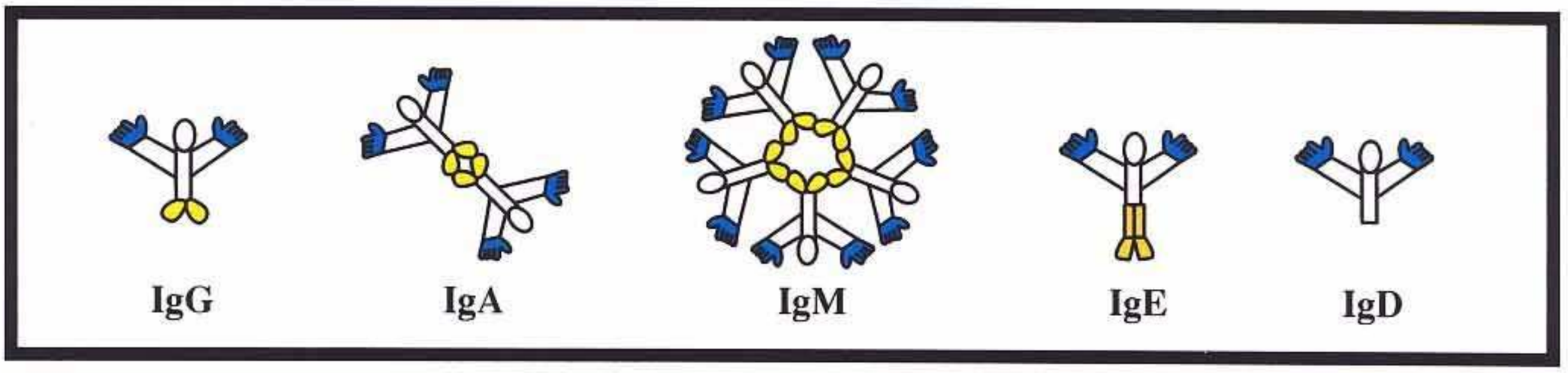


Strong disulphide bonds (shown in red), maintain the antibody's structure.



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

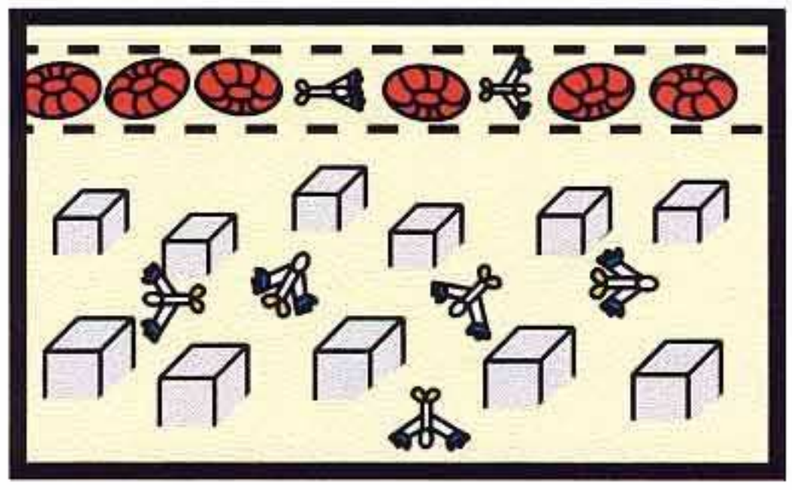
THE CLASS OF 5



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

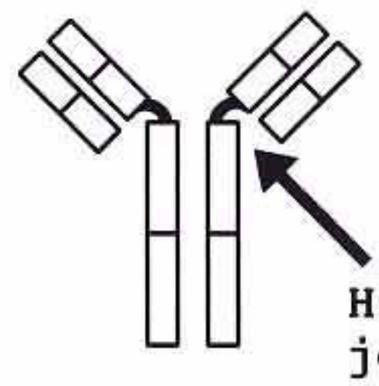
Fresh blood can be separated out into cells and plasma. Antibodies, a group of globular proteins found in the plasma, may be called "immunoglobulins" or Ig for short.

IgG

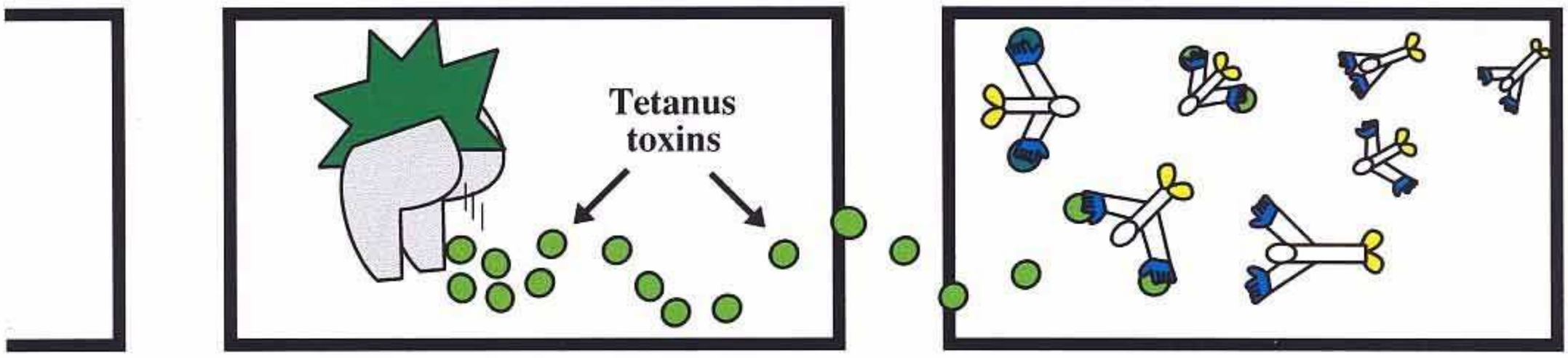


IgG are small enough to pass out of the blood and into the tissues.

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



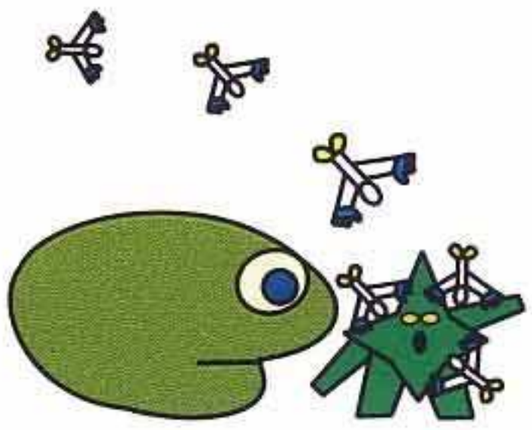
Newborn babies start making IgG after about 4 months.
In the adult, it is the commonest antibody in the plasma.



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

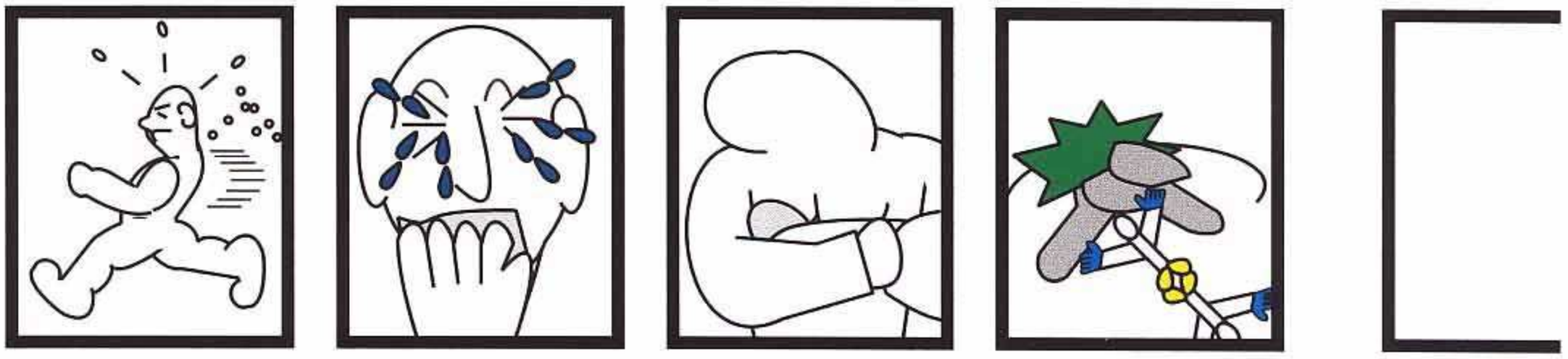
IgG are very effective at 'grabbing' these before they can do any harm.

2 IgG attached very close together, will activate complement.

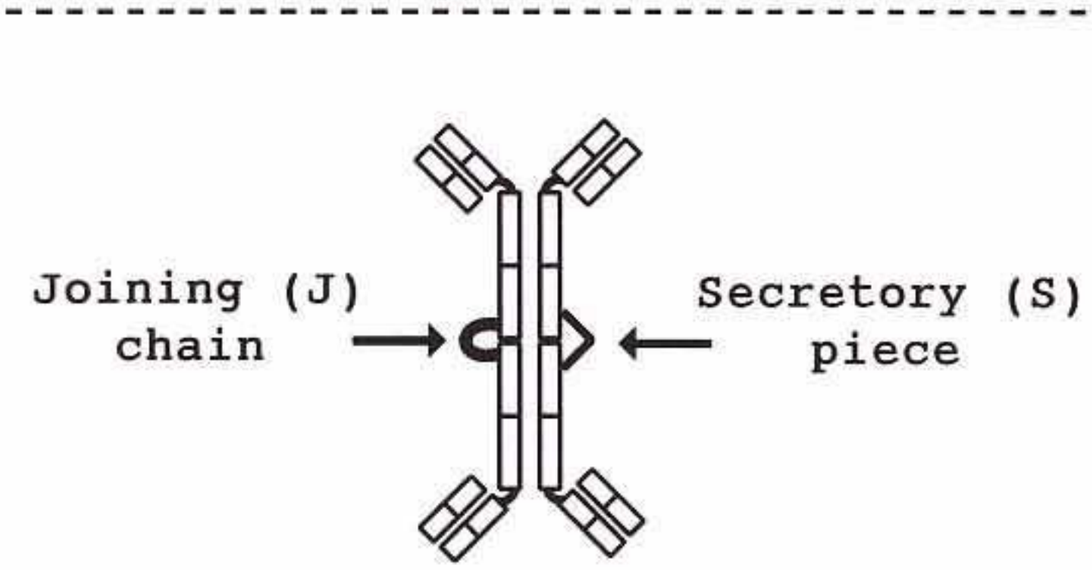


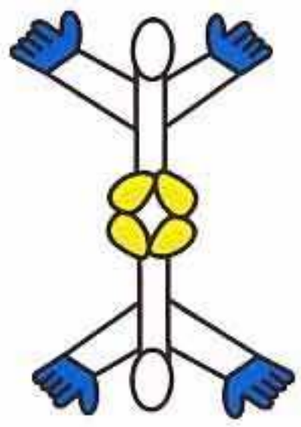
When attached onto anything, IgG 'feet' help immune cells to 'eat' foreign matter.

IgA

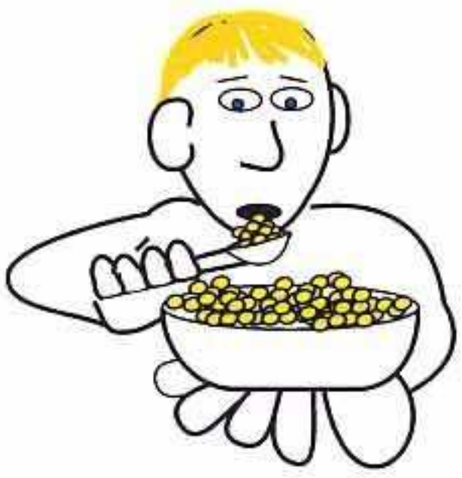


IgA antibodies are not found in the blood. They are secreted onto the surface of the body, in things such as:- sweat, tears, a mother's breast milk and mucus.





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

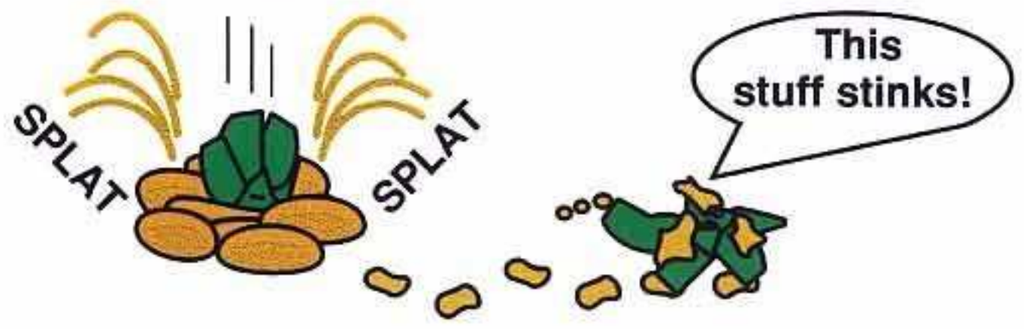


HE DOESN'T REALISE HIS MEAL IS CONTAMINATED

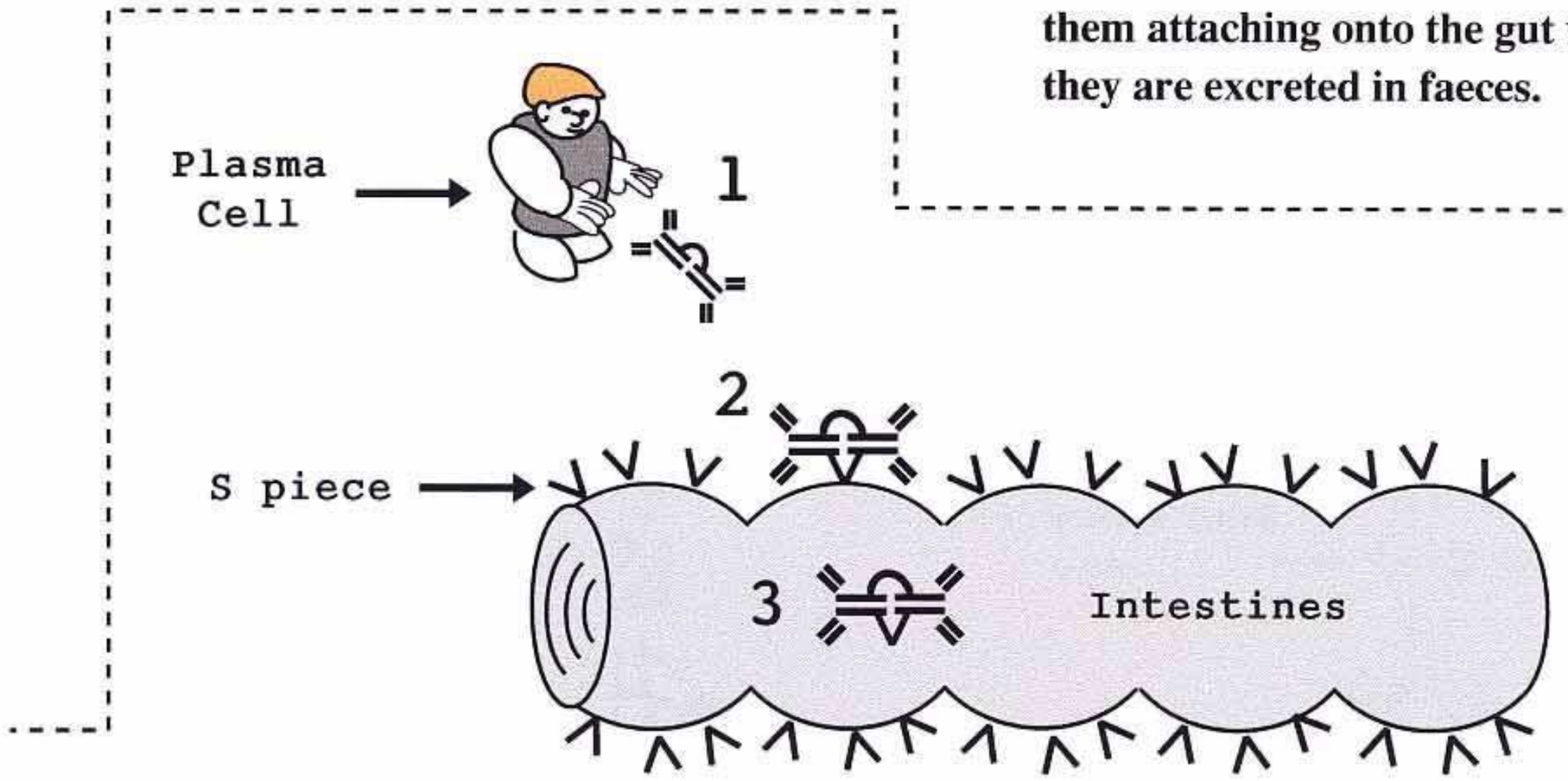
INSIDE HIS INTESTINE (INFECTION)

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

INSIDE HIS INTESTINE (IMMUNITY)

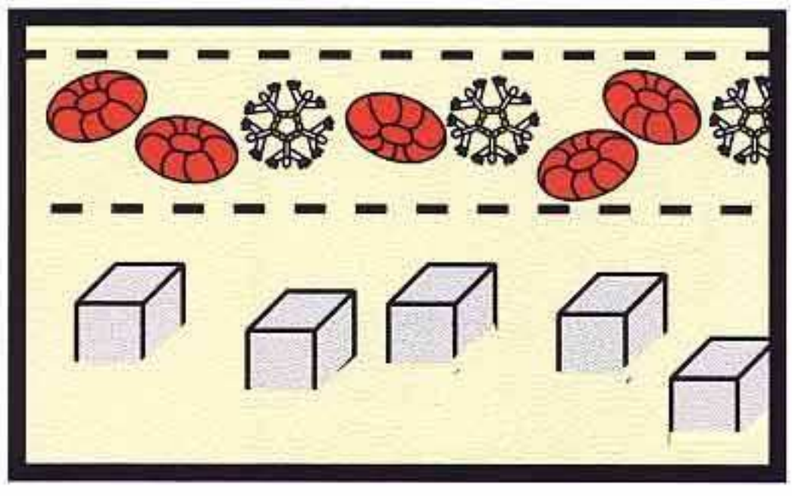


IgA 'grab' the microbes. This stops them attaching onto the gut wall and they are excreted in faeces.

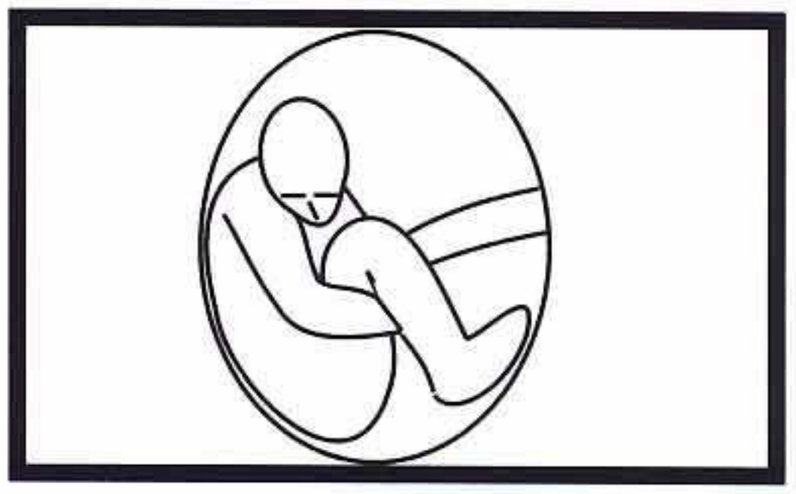


1. Plasma cells release IgA antibodies.
2. The IgA then attaches onto an S piece, lining the 'outer' gut wall.
3. The S piece then transports the IgA through and into the intestines.

IgM



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



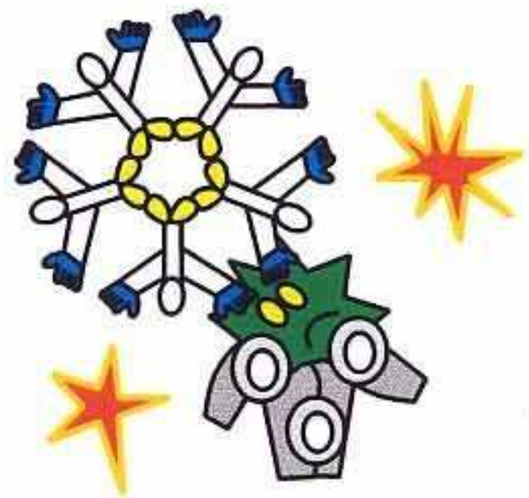
An unborn foetus will start to make this class of antibody at around 5 months gestation.

C Joining (J) chain

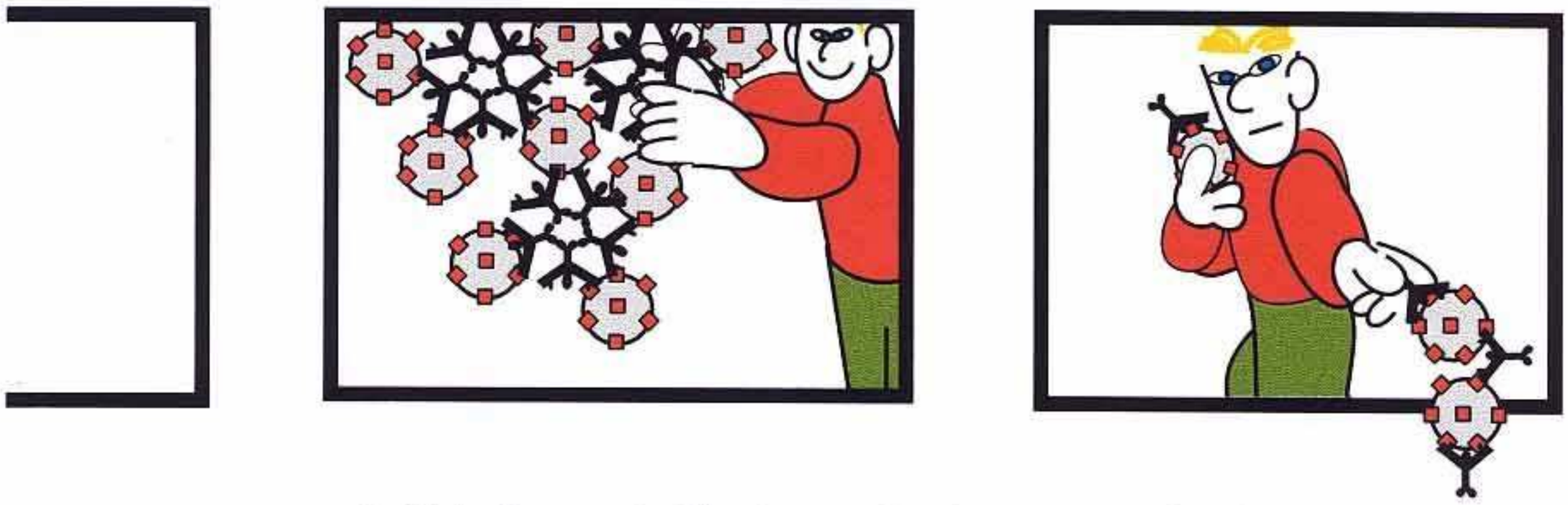
Disulphide bonds

* No hinge joints

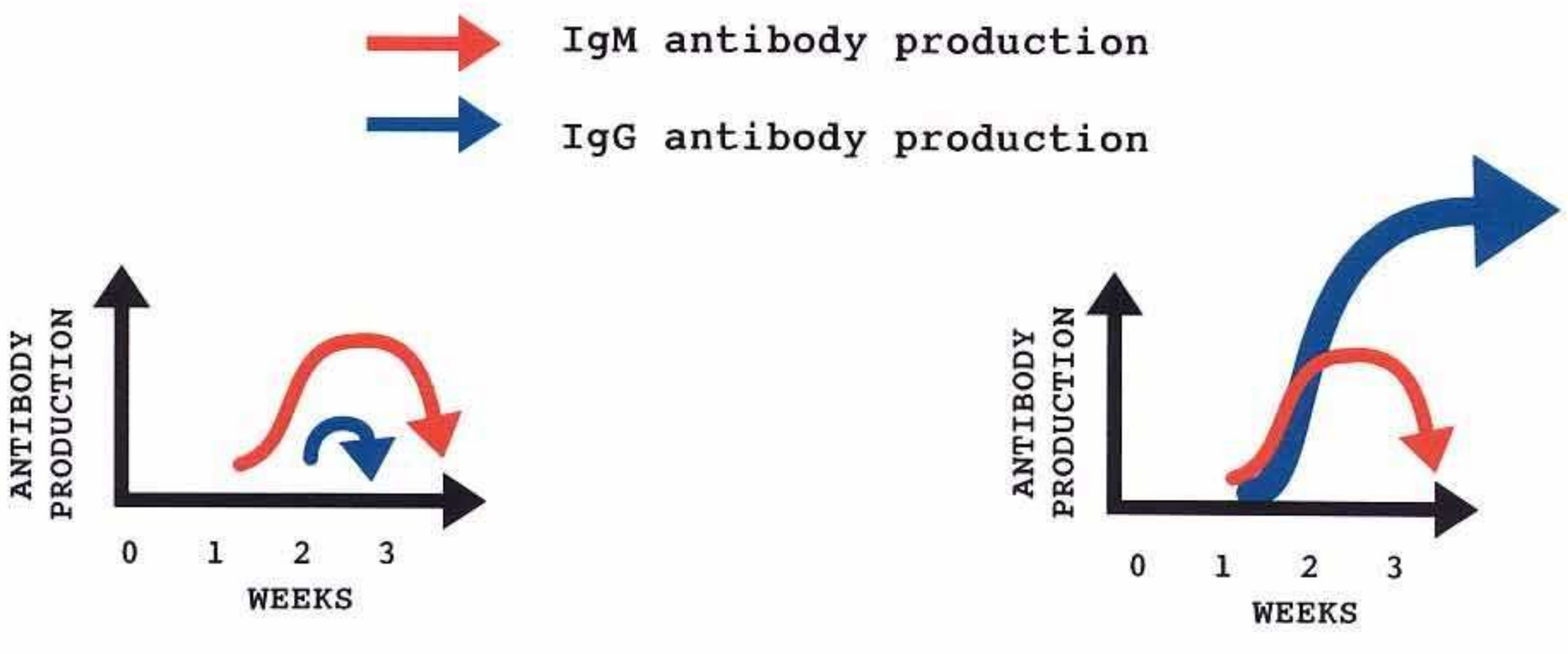
* 10 identical 'hands'



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

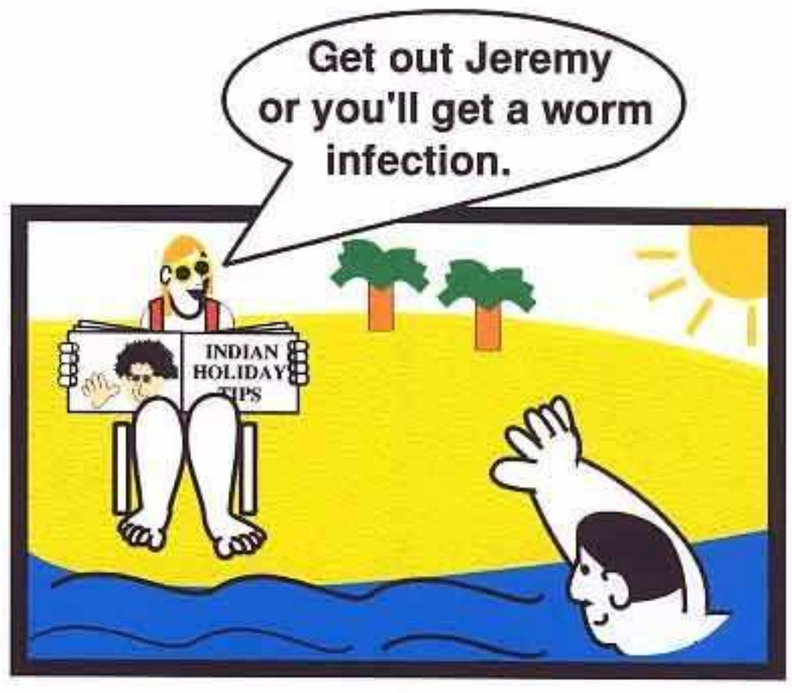
When foreign matter appears for the first time, mostly IgM antibodies are released.

SECONDARY RESPONSE

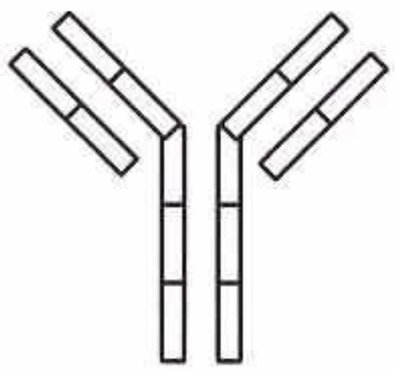
But if the same thing reappears:- IgM response remains unaltered. IgG response greatly increases.

IgE

Unfortunately, IgE antibodies can trigger violent, allergic reactions.



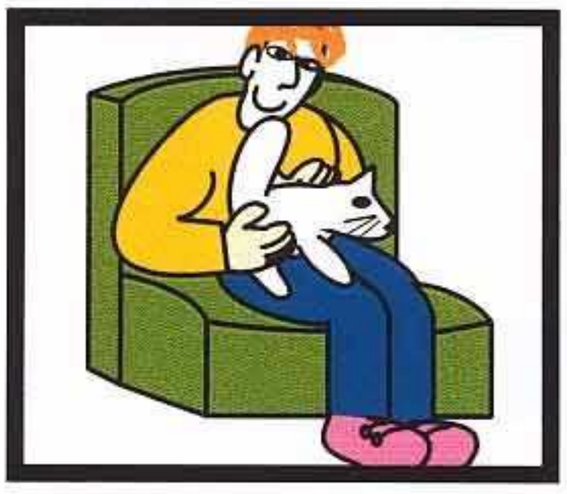
However, these antibodies do help to eliminate parasitic infections.



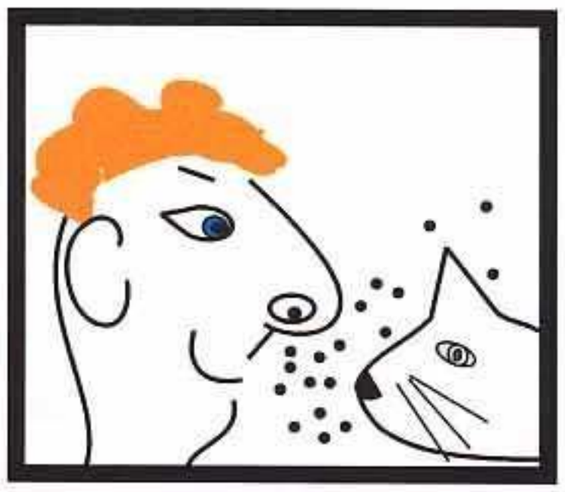
The IgE antibody does not have any hinge joints, so their 'arms' cannot move.

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

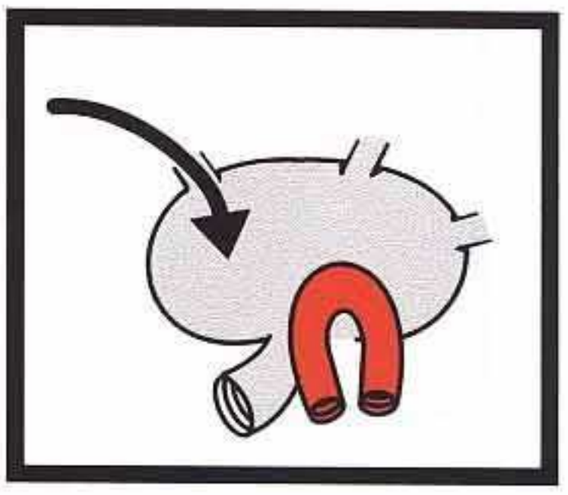
ALLERGY



Paul is stoking a cat.

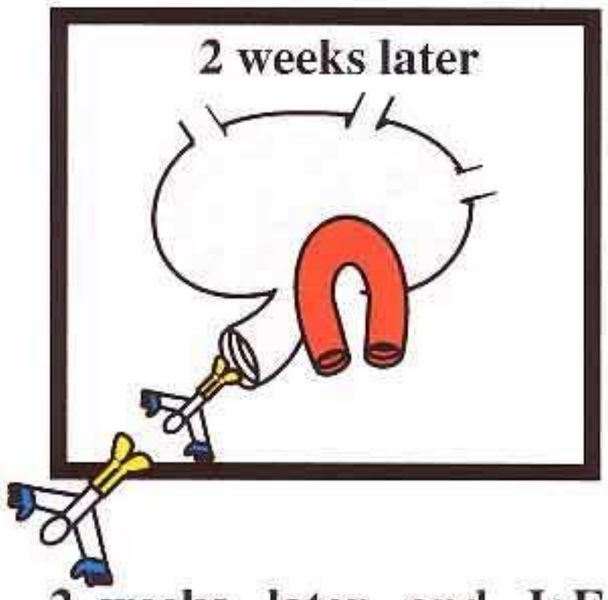


Particles from the cat are soon being inhailed.

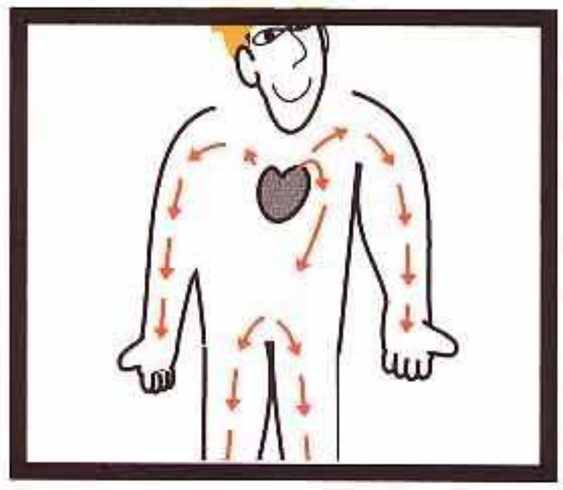


Some of these end up entering a lymph node.

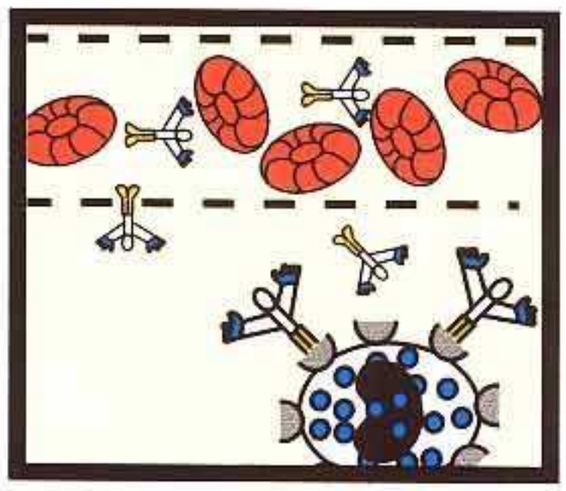
THE CAT IS LONG GONE!



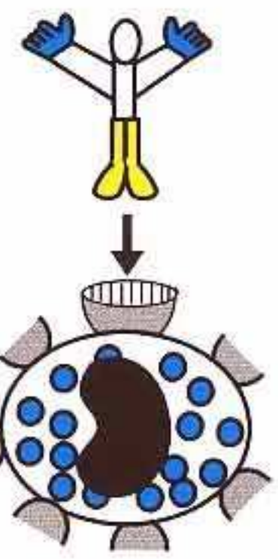
2 weeks later and IgE antibodies start to appear from the lymph node.



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

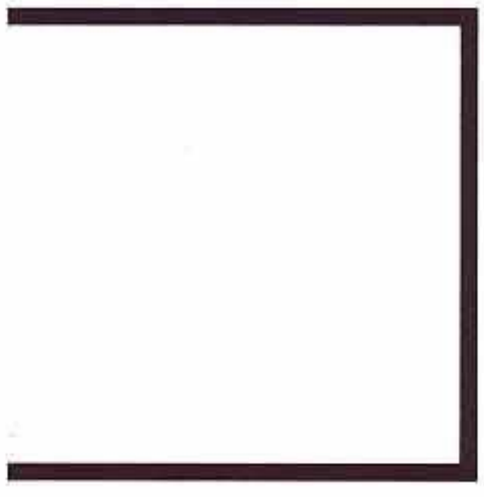


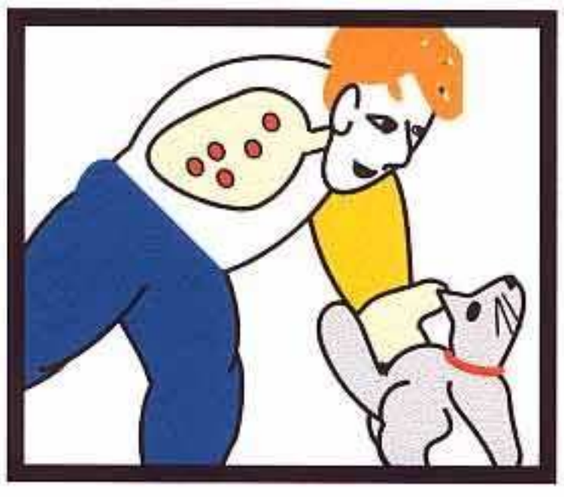
In the tissues, the anti-cat IgE attach onto mast cells using their 'special boots'.



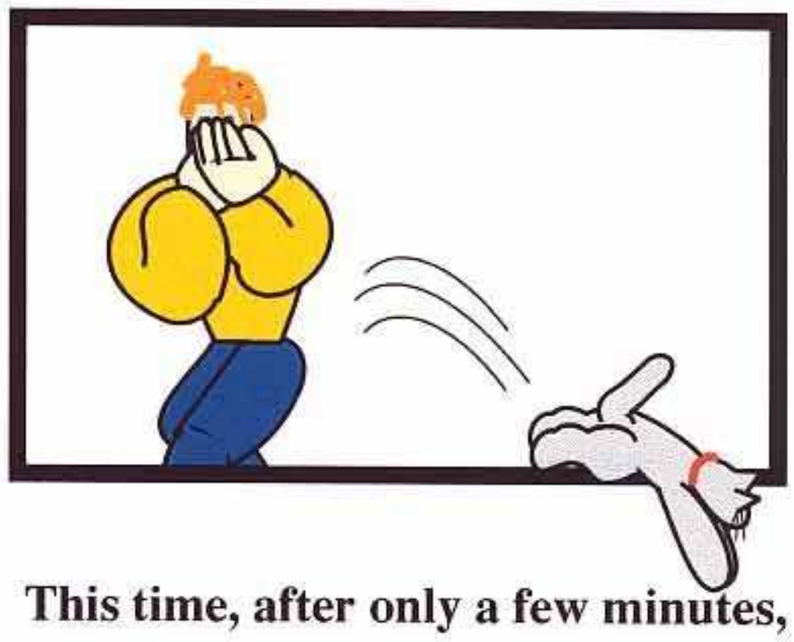
A mast cell has a bean-shaped nucleus, granules which contain histamine and their surface is coated in IgE 'boot' receptors.

WEEKS LATER, PAUL MEETS ANOTHER CAT

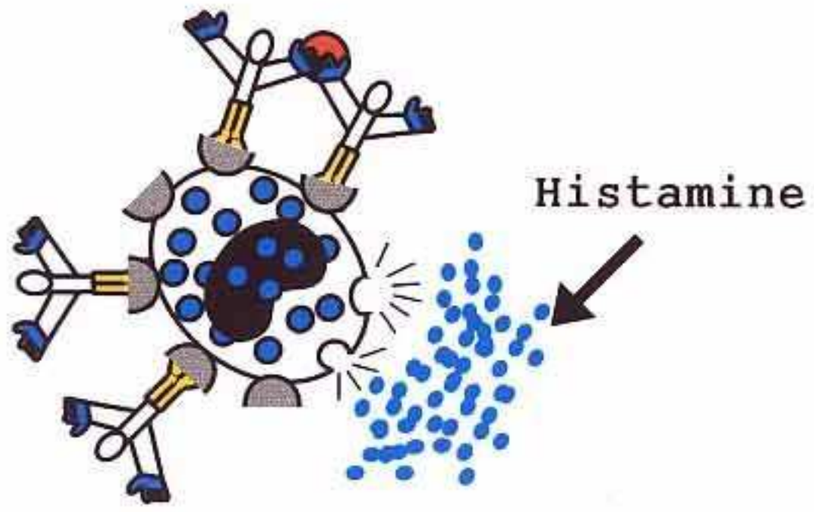




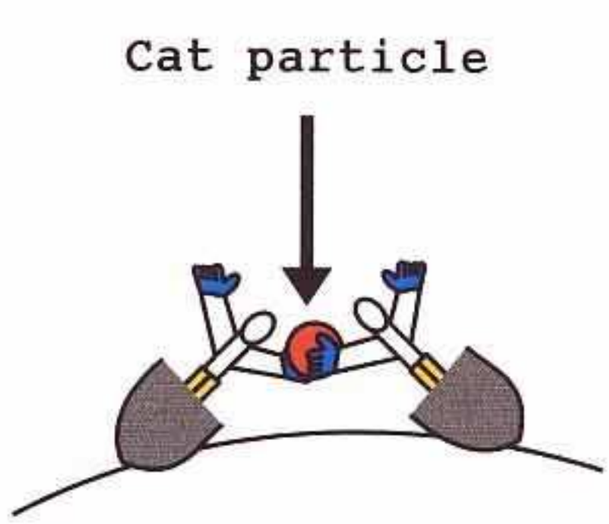
Cat particles again enter his lungs.



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



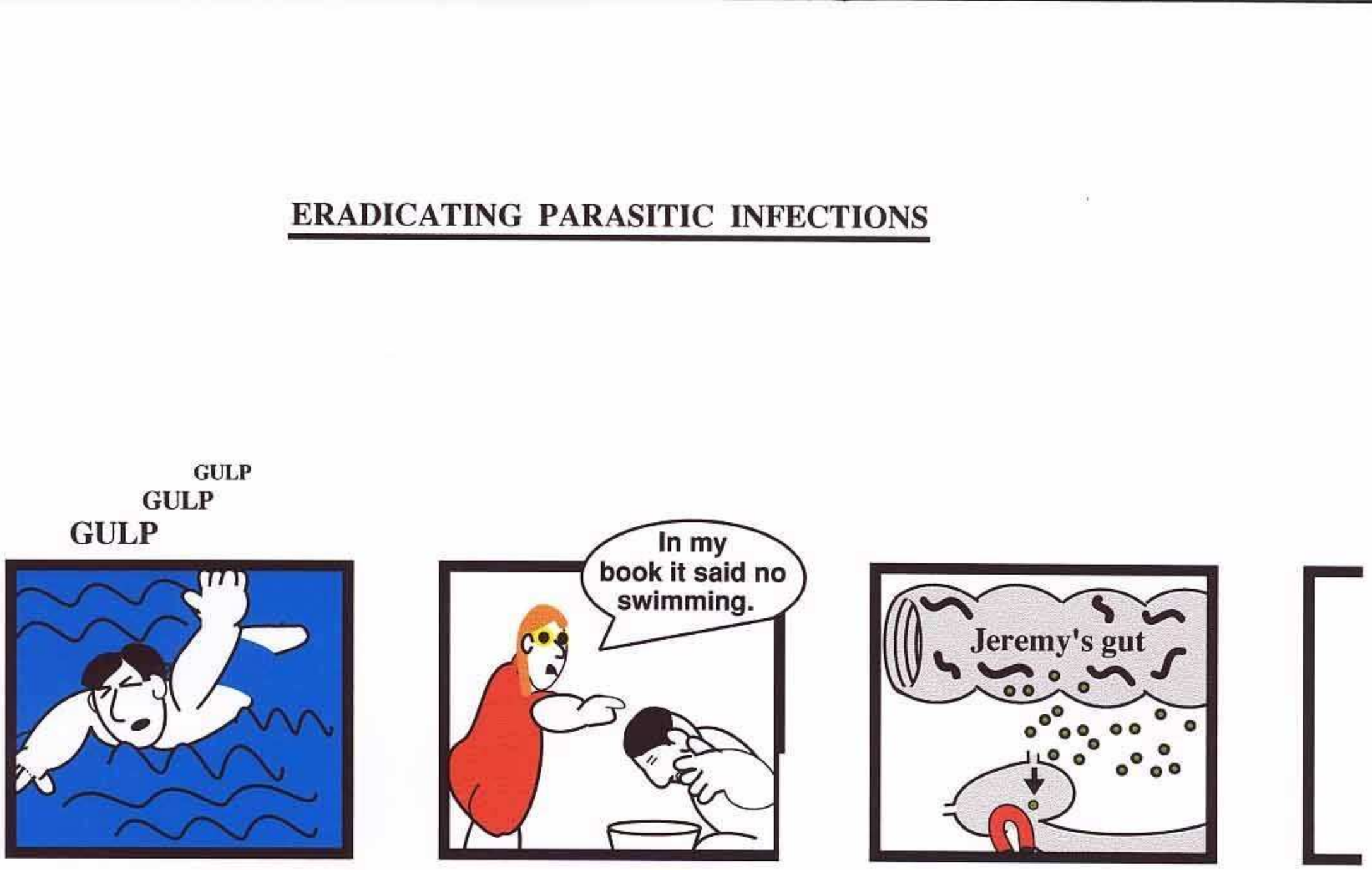
Mast cells close to the lungs, were triggered into releasing histamine, which initiated a violent inflammatory response.



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).

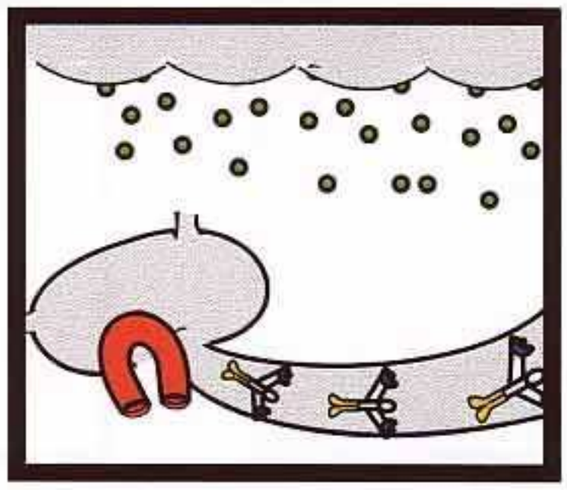
ERADICATING PARASITIC INFECTIONS



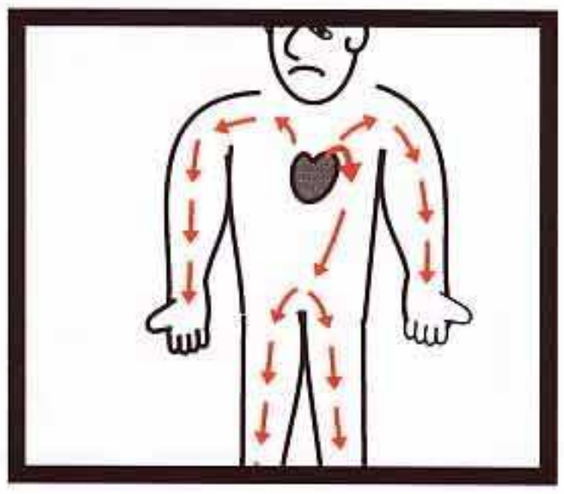
Jeremy swallows some contaminated water.

Not long after, worms begin to replicate inside him.

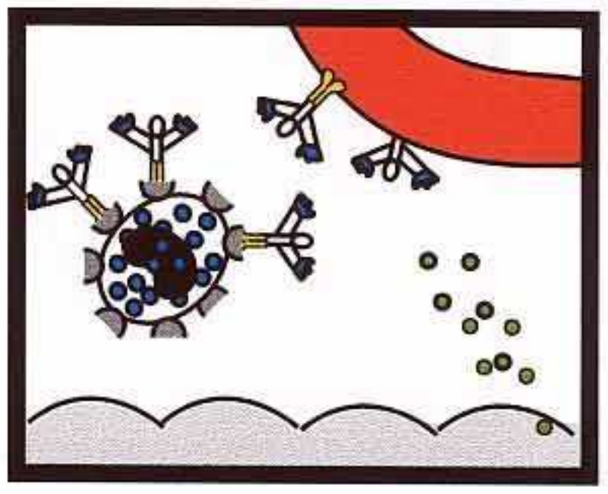
Worm particles reach a nearby lymph node.



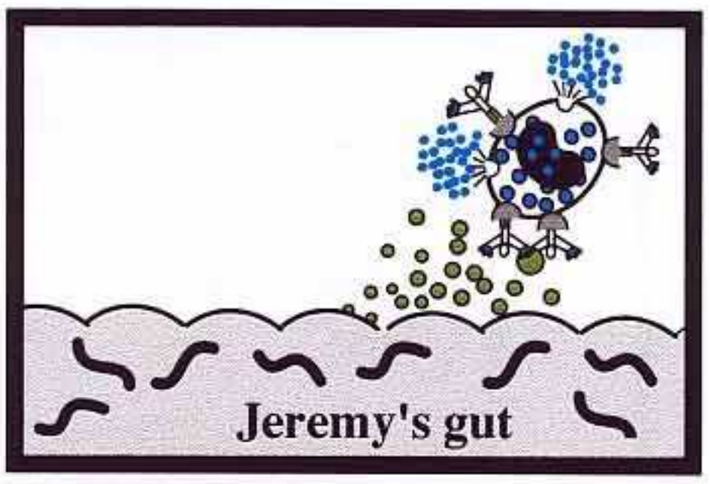
2 weeks later, anti-worm IgE start to appear from the lymph node.



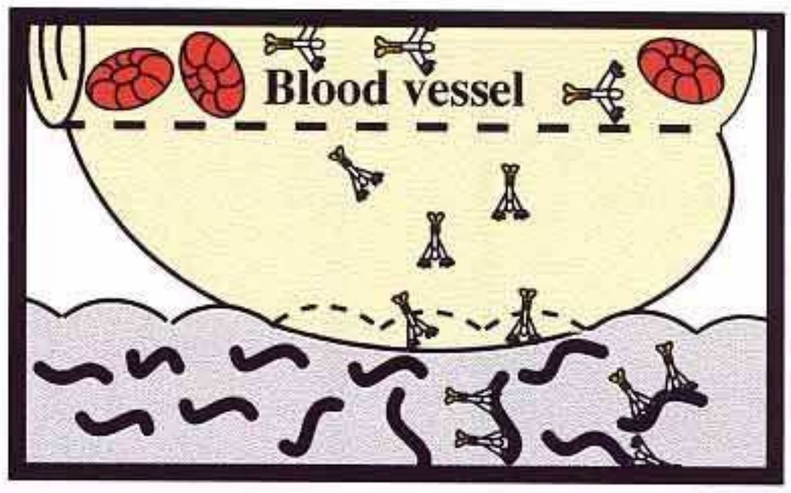
On entering his heart, the IgE are pumped around his body.



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.

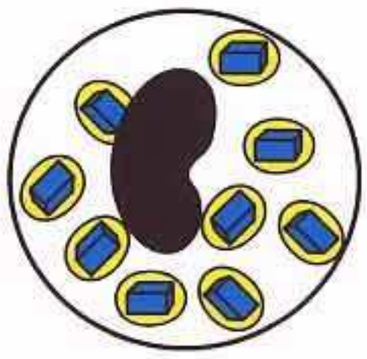
Inflammation is covered in greater detail in chapter 15.

MEET MR EOSINOPHIL

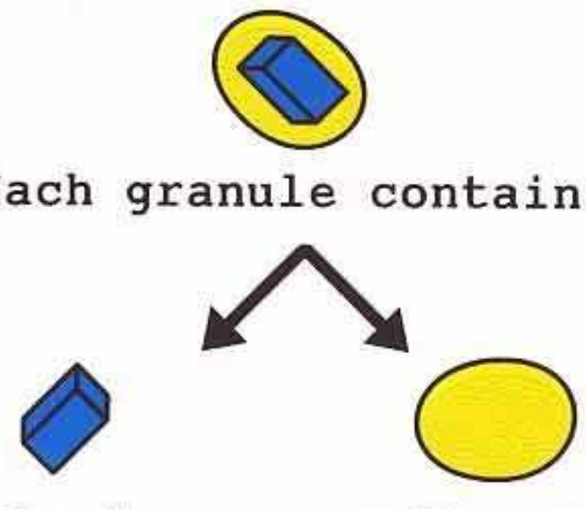
Mr Eosinophil, one of our white blood cells detects trouble.

So he goes to investigate.

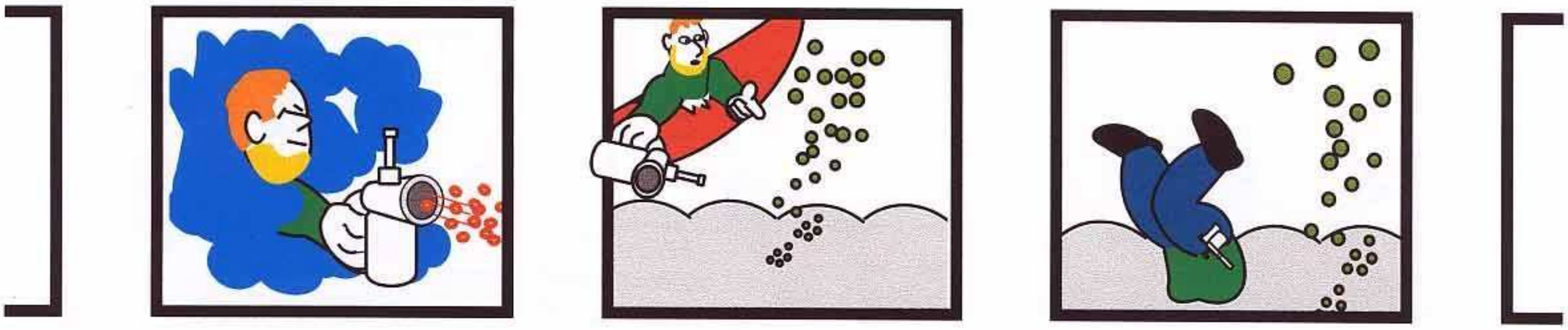
Soon he is squeezing out of the blood vessel.



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



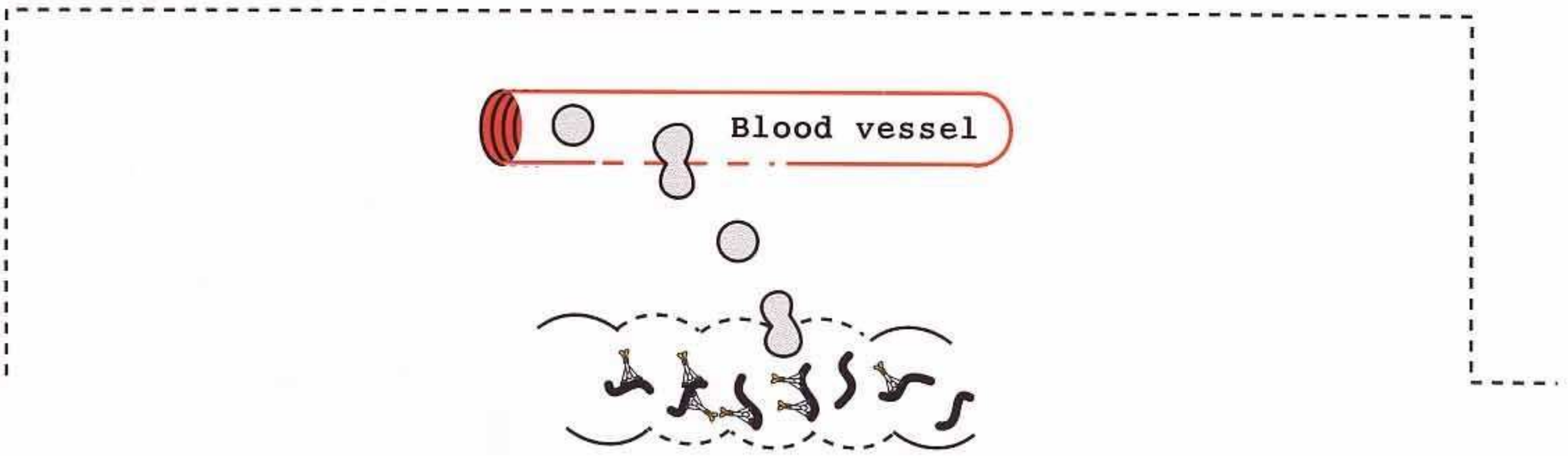
MR EOSINOPHIL EMERGES INTO A DENSE INFLAMMATORY FOG



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.

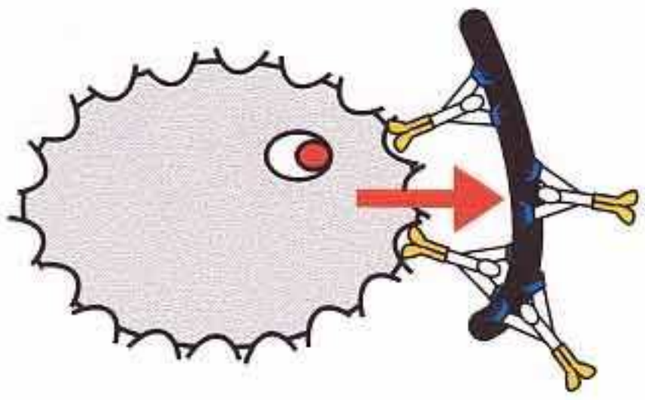


Attracted by factors from the mast cell, the eosinophil leaves the blood vessel, deactivates the histamine and then enters the gut.

MR EOSINOPHIL DROPS IN

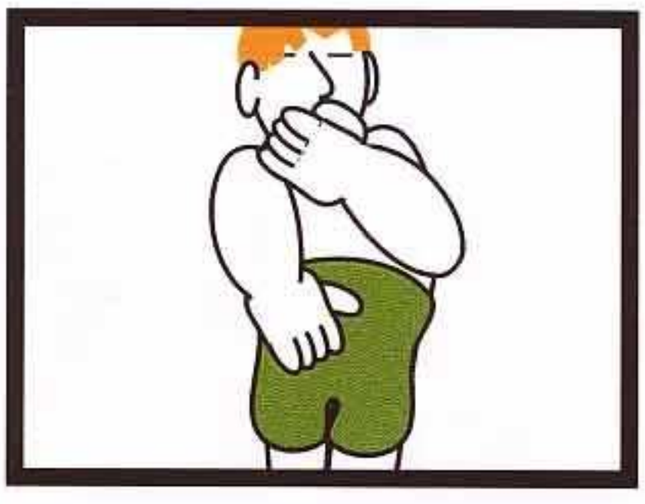
As Mr Eosinophil enters the gut, he 'sees' the problem.

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

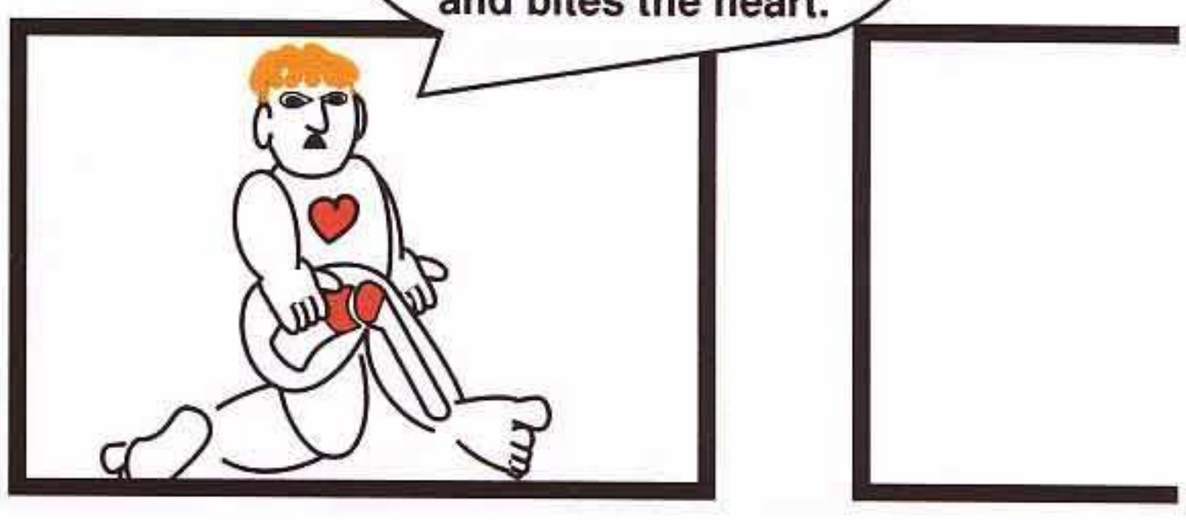


An eosinophil uses its surface IgE 'boot' receptors, to attach onto the parasite coated in IgE, before discharging its killing granules.

CAN YOUR ANTIBODIES HARM YOU?

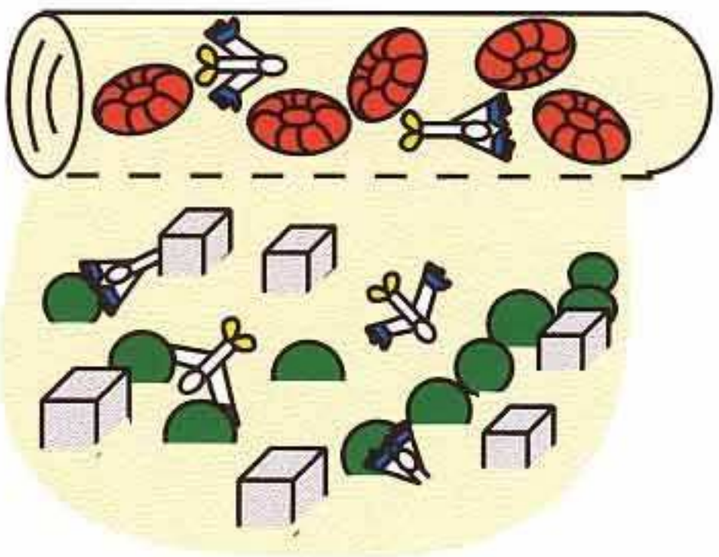


This young adolescent has a nasty cough and sore throat.

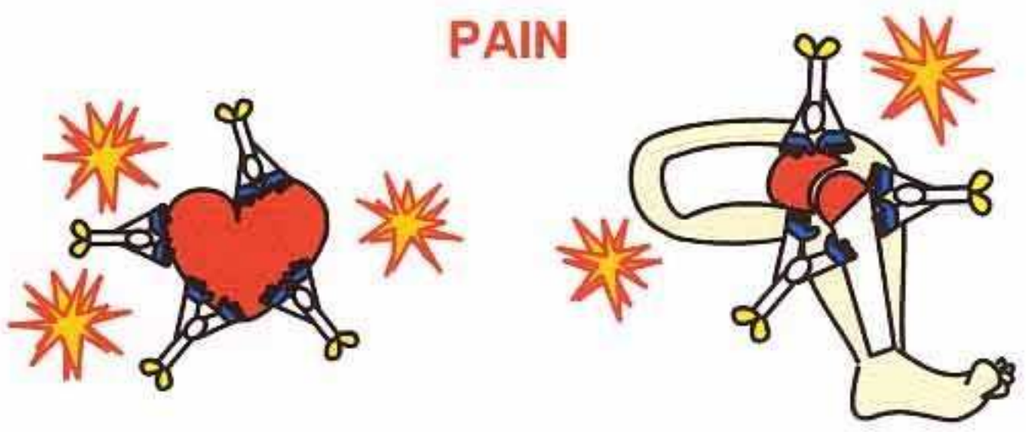


2 weeks later, he experiences severe heart and joint pains.

RHEUMATIC HEART DISEASE

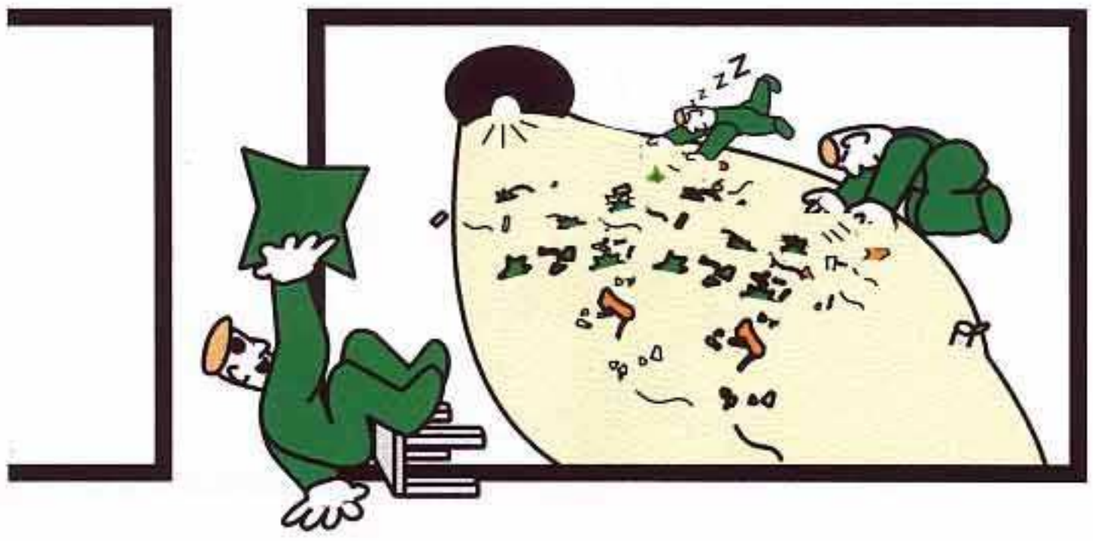


Antibodies arrive in the throat to eliminate the infection, by 'grabbing' the bacteria.

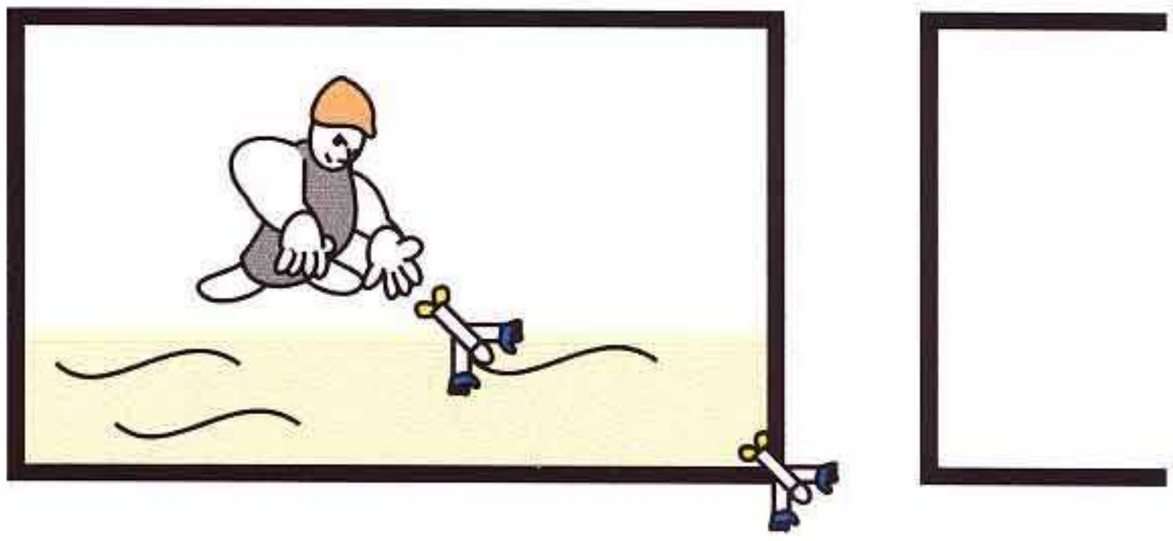


Unfortunately for this young boy, their 'hands' also fit his joints and heart muscle, which causes complement to be activated.

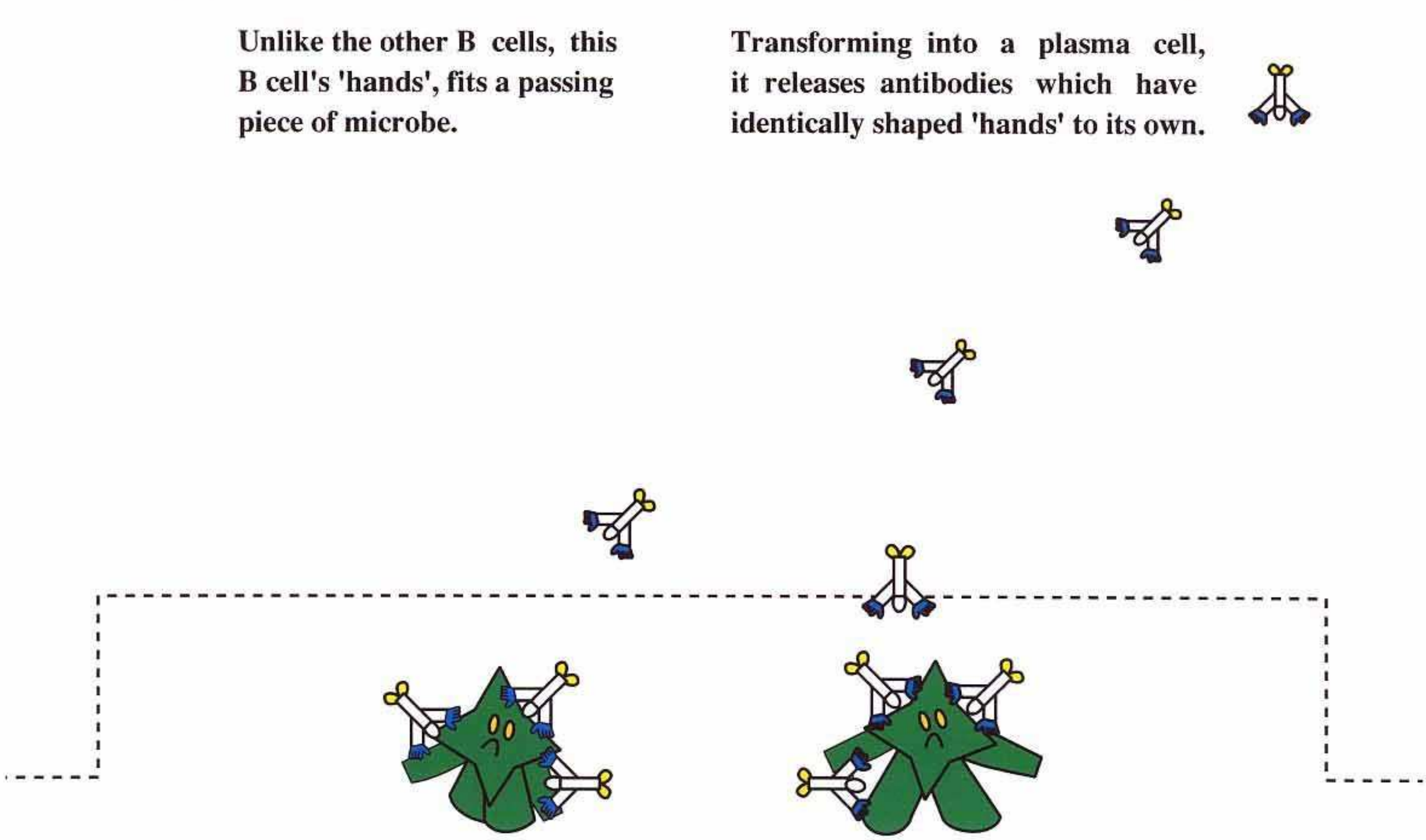
LUCKILY OUR ANTIBODIES RARELY HARM US



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



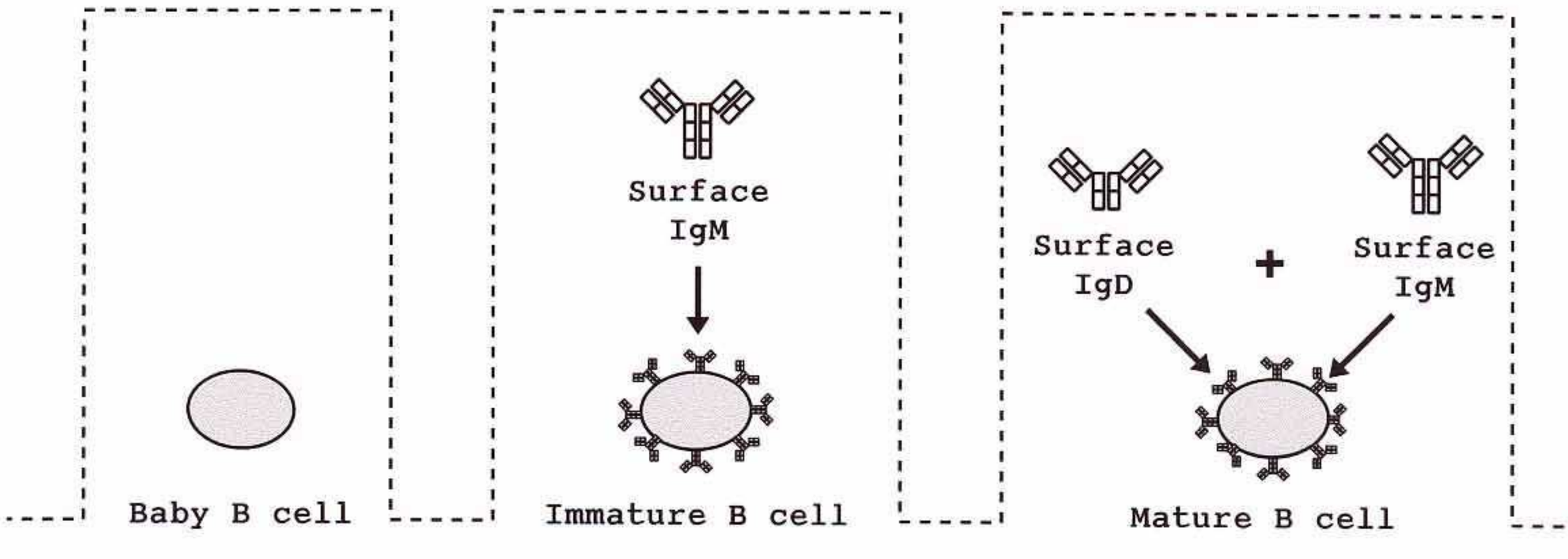
Transforming into a plasma cell, it releases antibodies which have identically shaped 'hands' to its own.



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

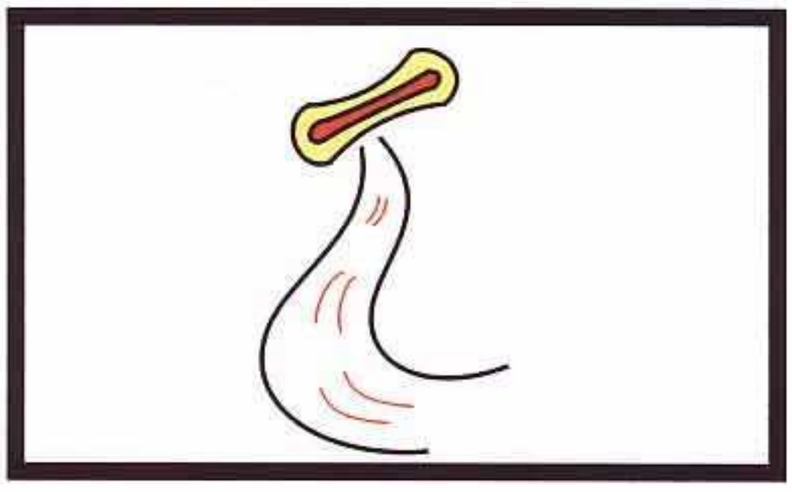
THE STORY STARTS BACK IN THE BONE MARROW

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).

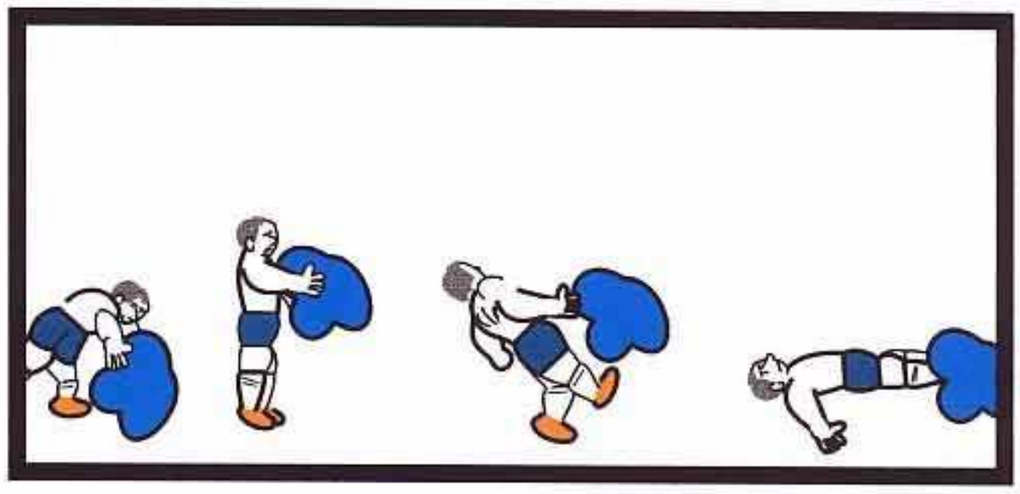


As the B cell matures inside the bone marrow, it expresses a range of surface antibodies.

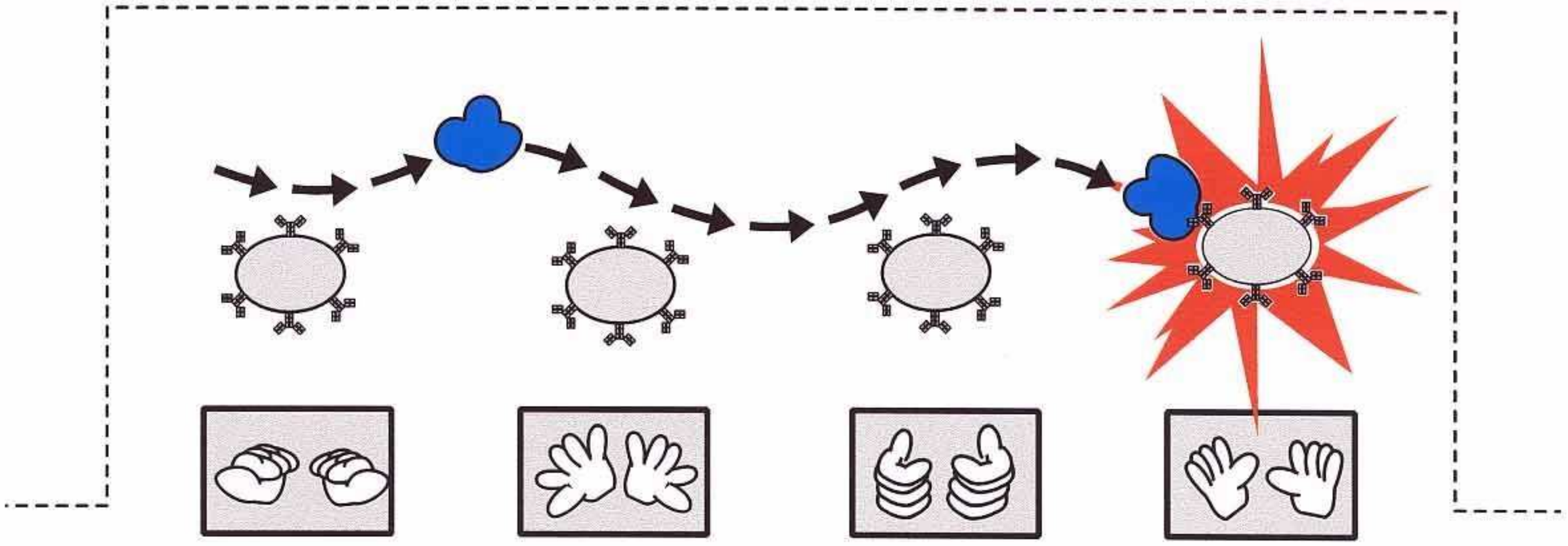
IT'S A QUESTION OF LIFE OR DEATH FOR THE YOUNG B CELL



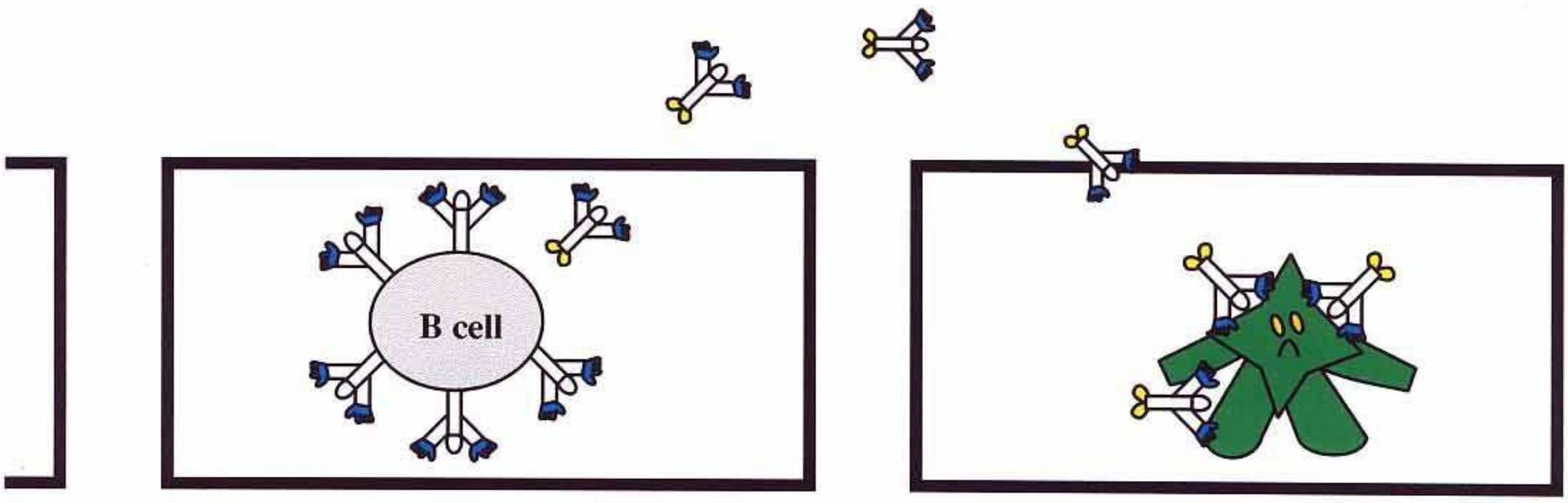
As bone marrow has a good blood supply, many fragments from around the body pass through it.



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



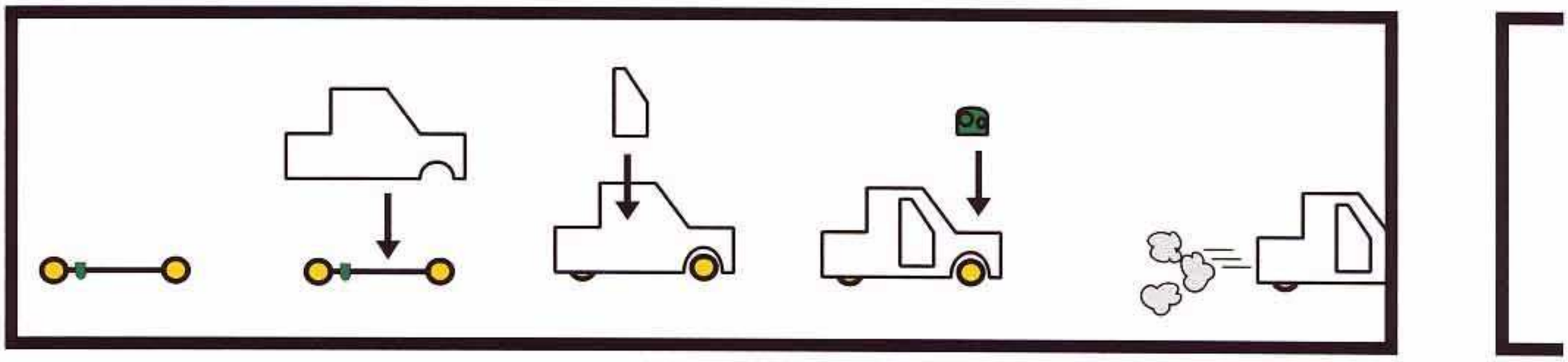
It appears that whilst immature B cells only express surface IgM antibodies, they are at risk of auto - destruction, should their unique fixed 'hand' shape fit anything.



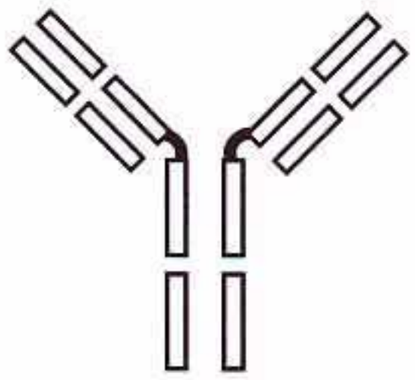
The 'hand' shape of a B cell's surface antibodies, are identical to the antibodies it releases.

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

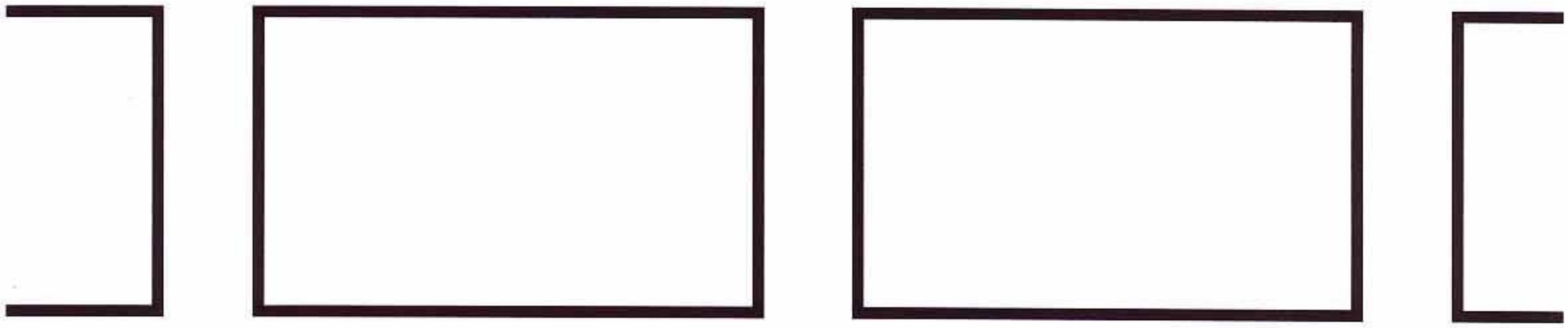


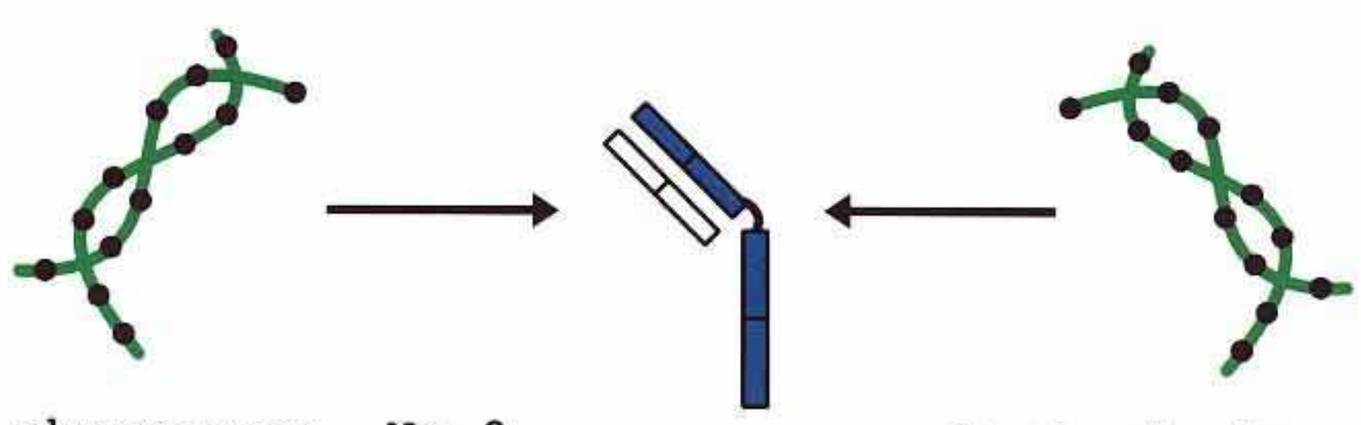
Parts are bolted together to produce the finished article.



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

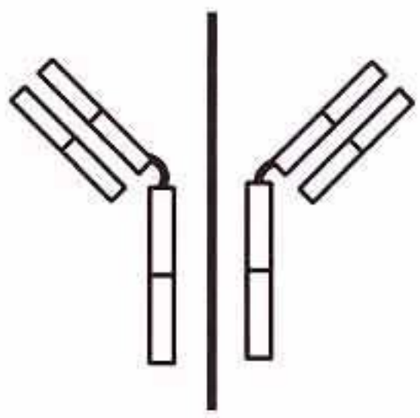
EVERY NUCLEATED CELL IN THE BODY CONTAINS 23 PAIRS OF CHROMOSOMES





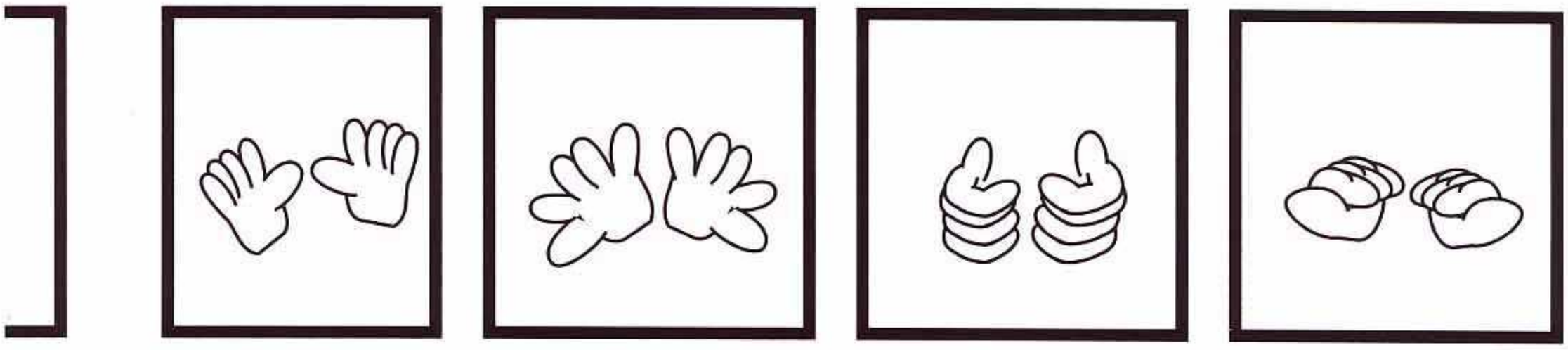
Part of chromosome No.2, codes for the light chain.

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

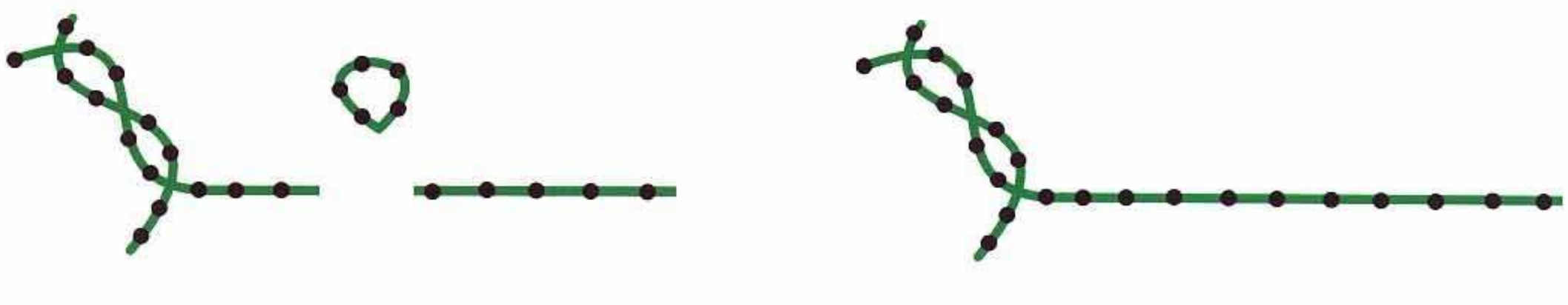


Then 2 identical halves are 'bolted' together.

HERE ARE 4 FIXED ANTIBODY 'HAND' SHAPES

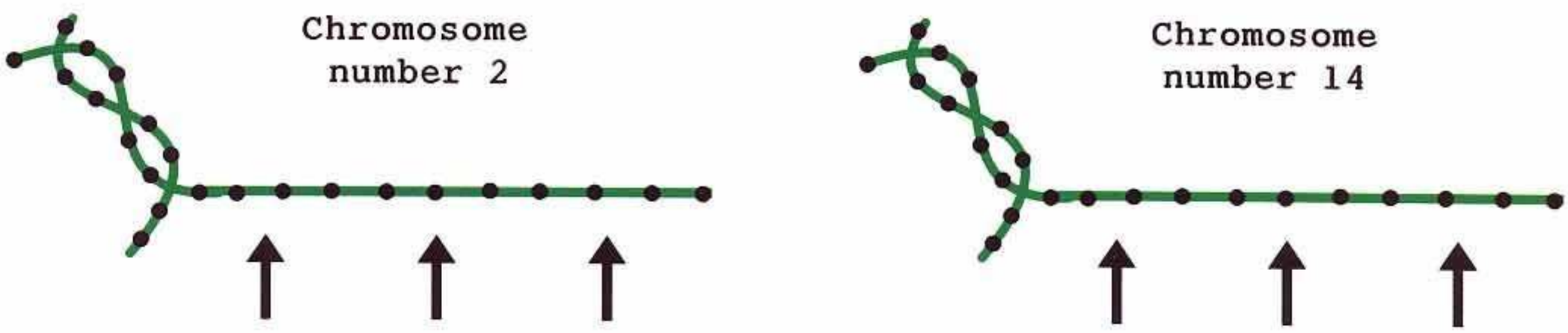


HOW B CELLS ACQUIRE THEIR UNIQUE 'HAND' SHAPE

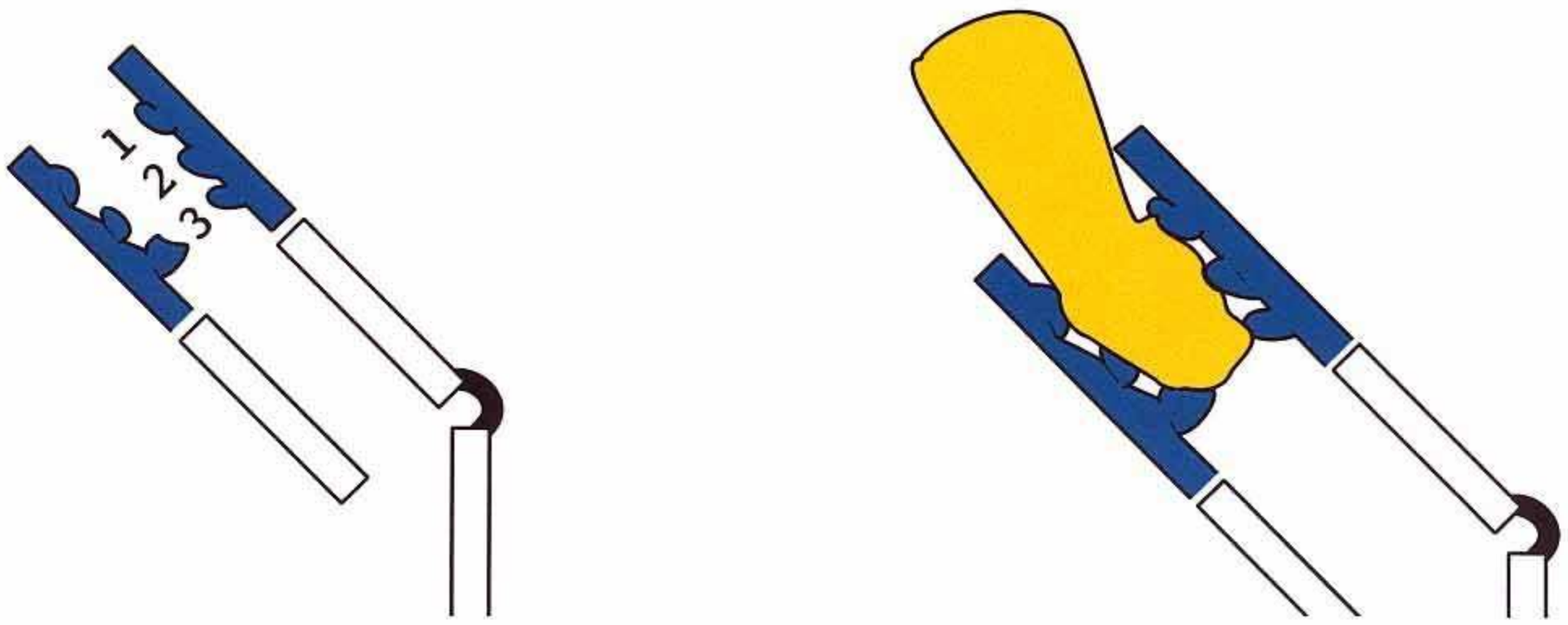


As an immature B cell develops, some of the genes capable of coding for the 'hand' shape, are randomly removed by recombinase enzymes.

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



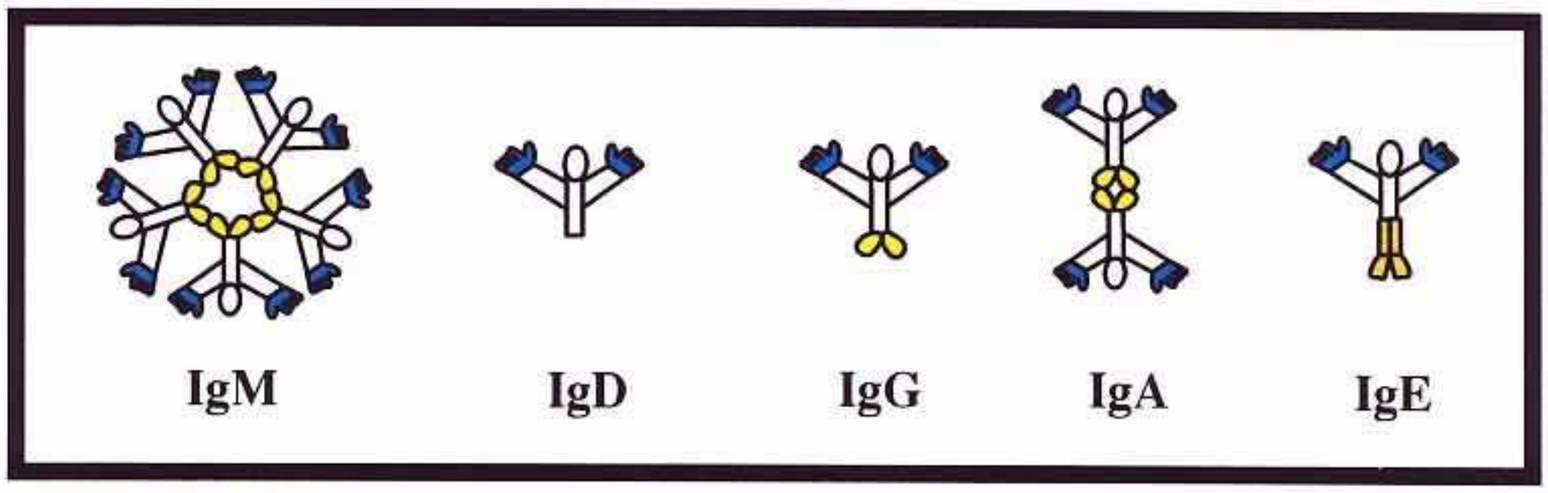
Genes are randomly removed from 3 specific areas along both chromosomes.



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.

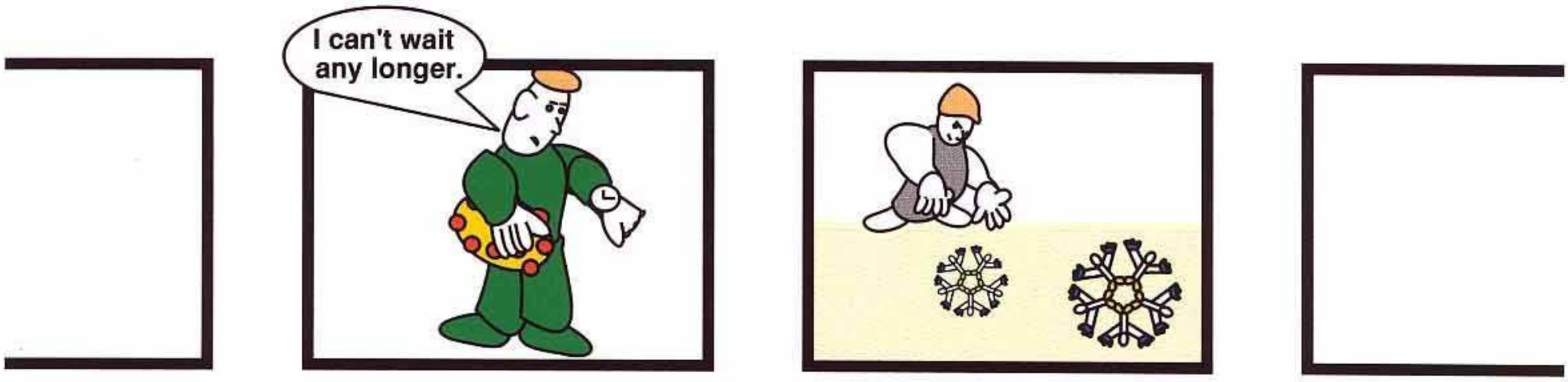
WHO CARES ABOUT CLASS?



There are 5 classes of antibody.

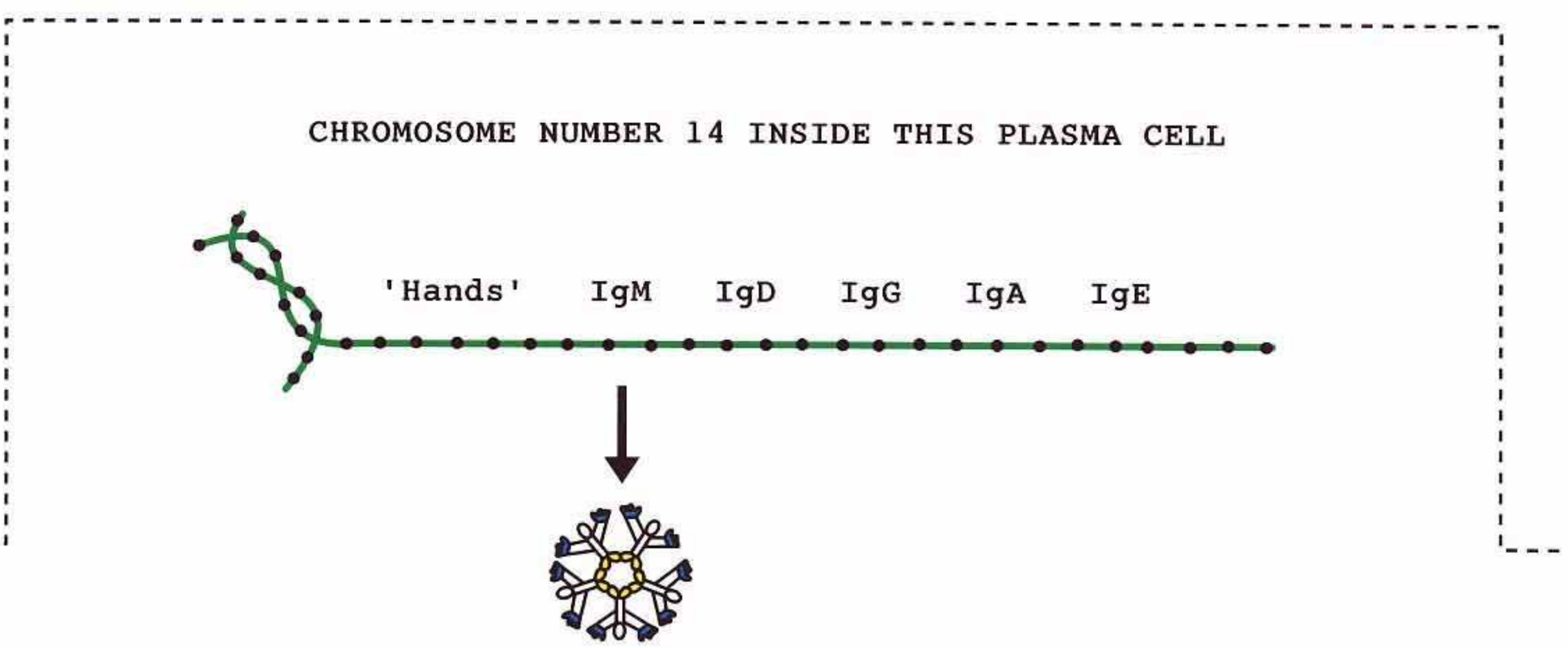
Soluble substances which allow cells to communicate with each other, are sometimes called "cytokines".

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.

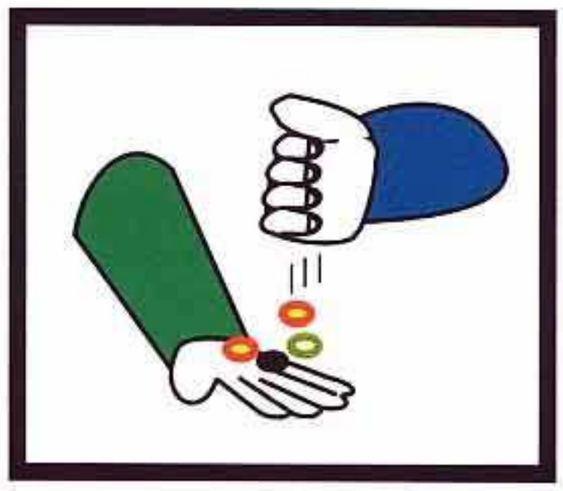
So after transforming into a plasma cell, he starts to release IgM antibodies.



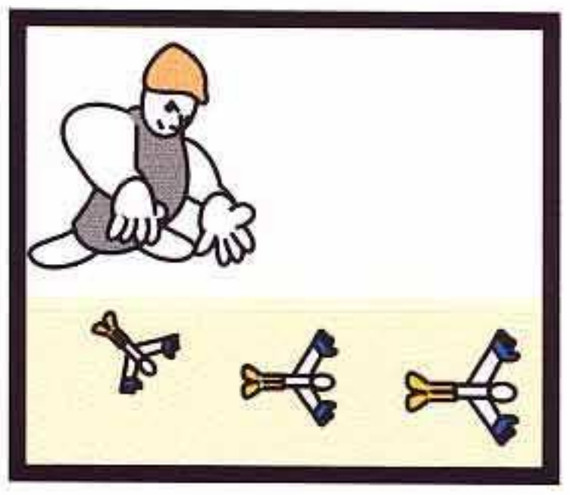
The genes next to those coding for the 'hand' shape, are switched on.

IF A USEFUL T HELPER DOES ARRIVE

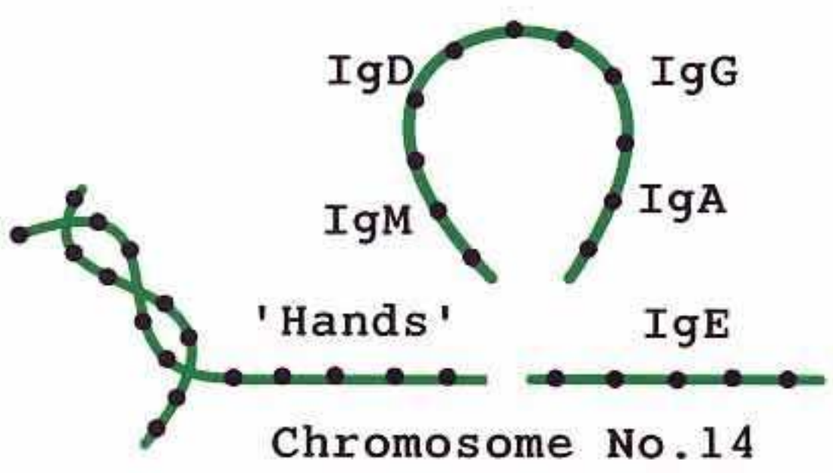
This time a T helper arrives, whose 'hand' shape also fits the same object.



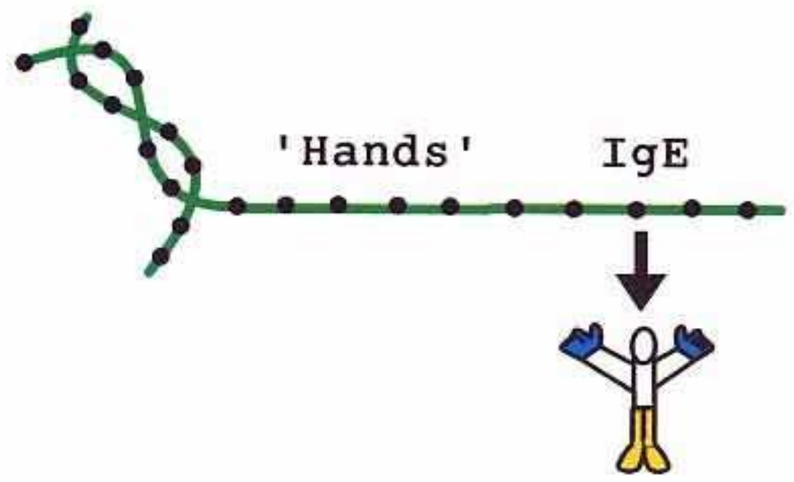
The T helper now releases factors, to make the B cell produce IgE antibodies.



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

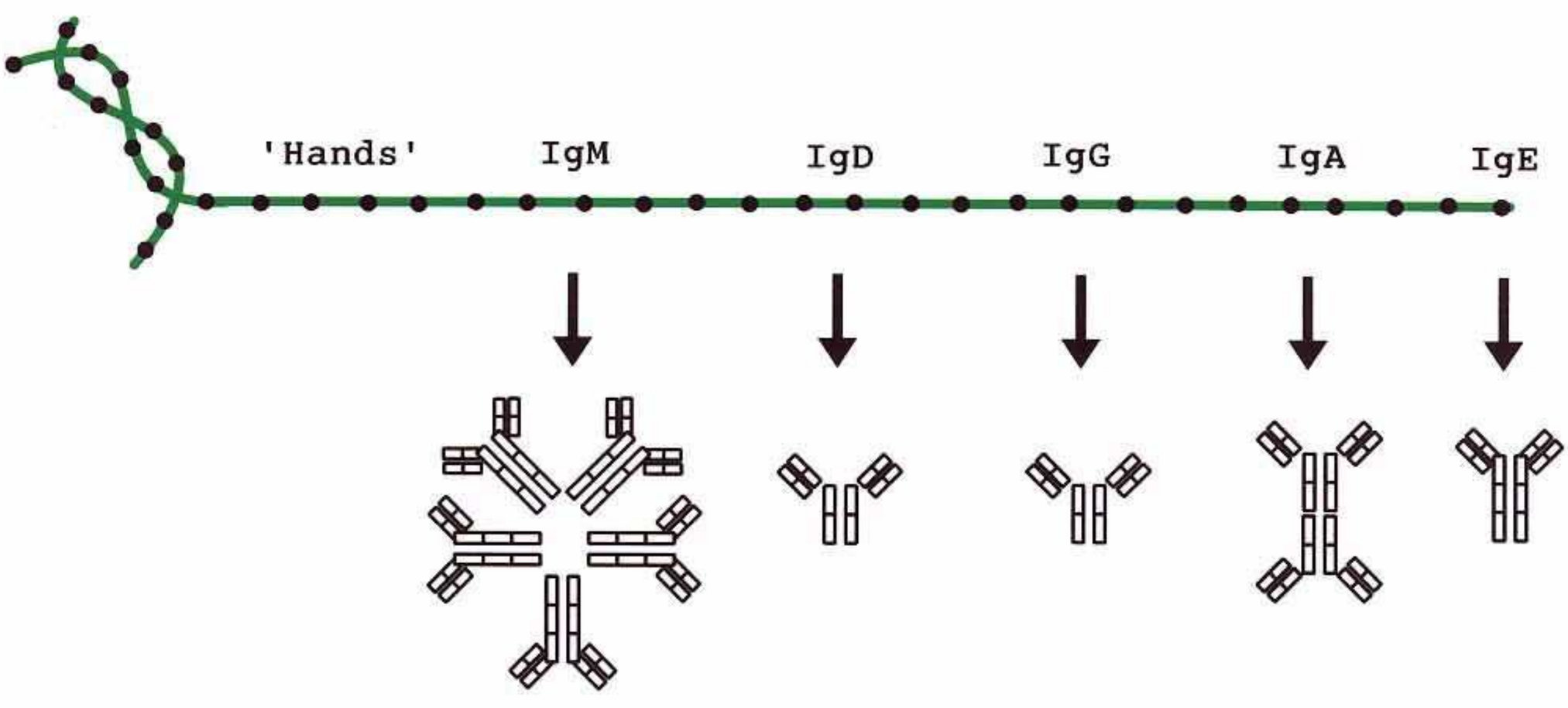


The cytokines from the T helper, trigger enzymes inside the B cell, to remove specific genes along chromosome number 14.



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.

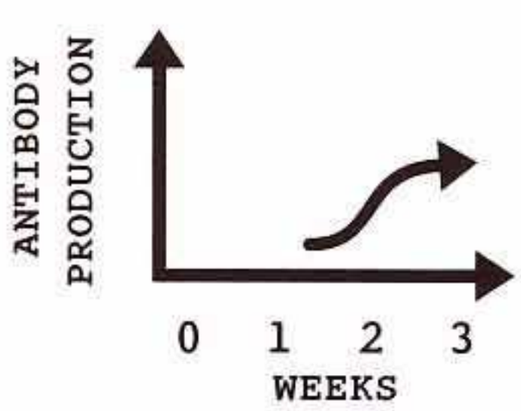
If the T helper releases IL-2, IL-5 and TGF.....IgA are produced.

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

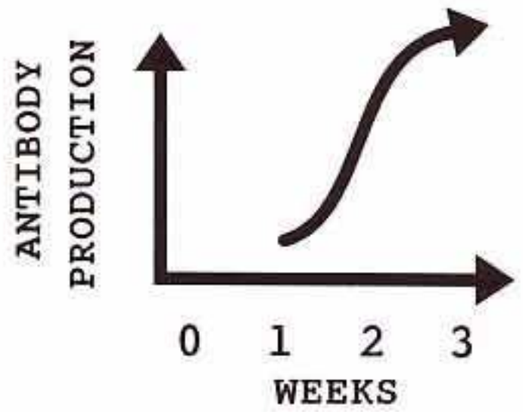
*IgD antibodies are normally only found attached to the surface of B cells and are not actively secreted into the blood.

THE CLONAL SELECTION THEORY

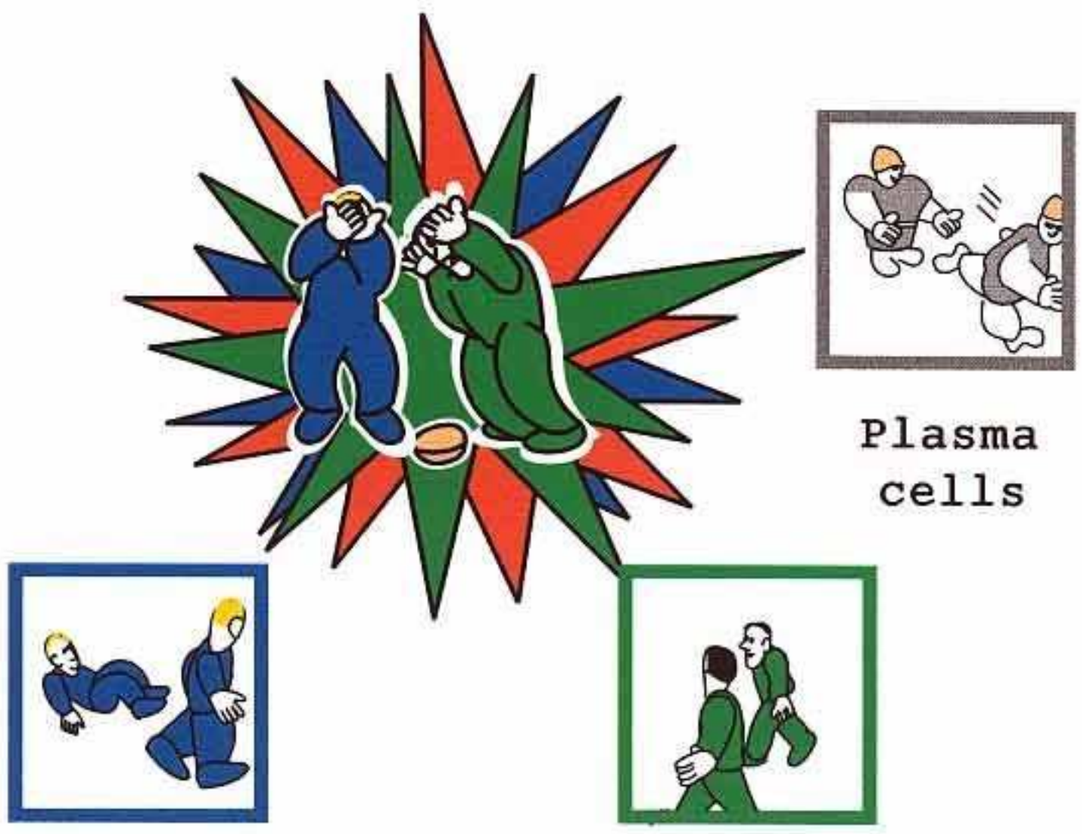
PRIMARY RESPONSE



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!