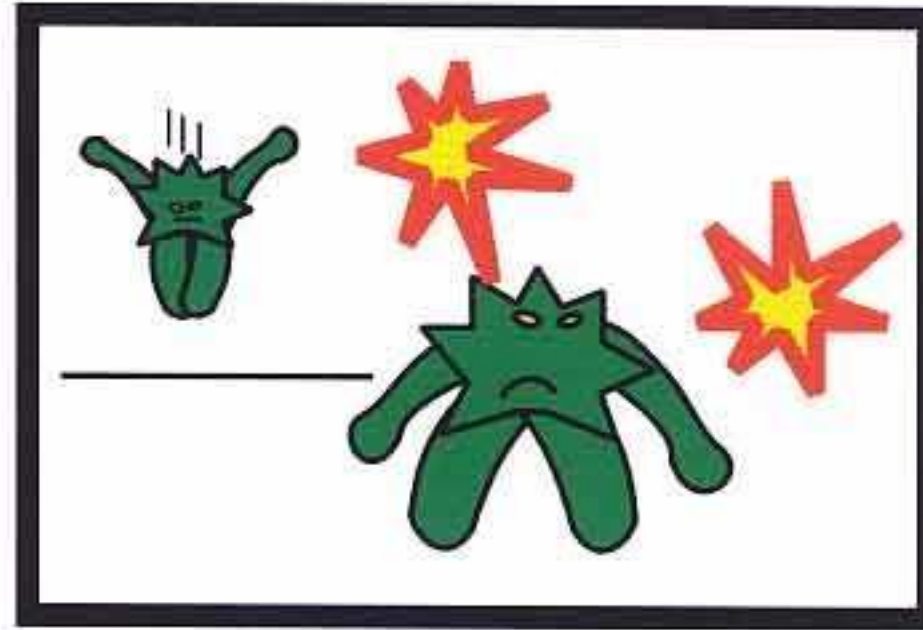


CHAPTER FOURTEEN

COMPLEMENT



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



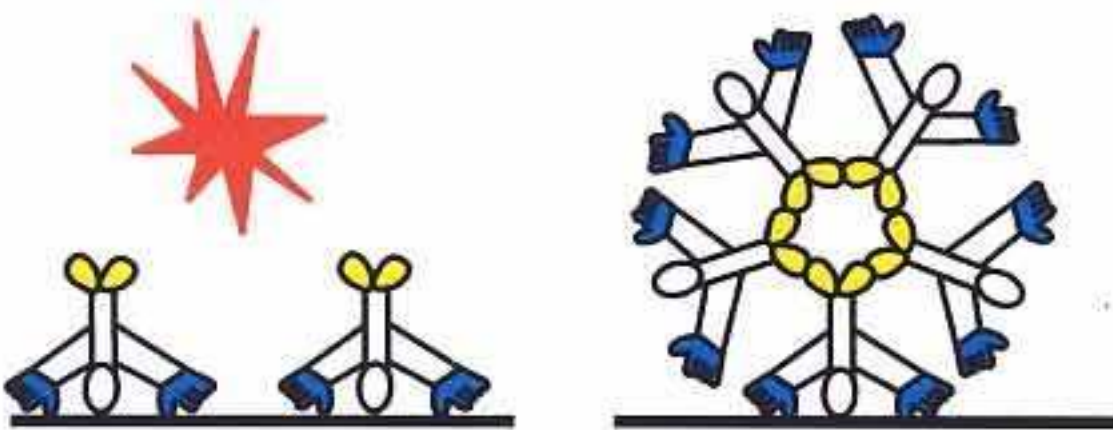
Likewise, when complement is activated, it warns the immune system of invading microbes.



Easy reading

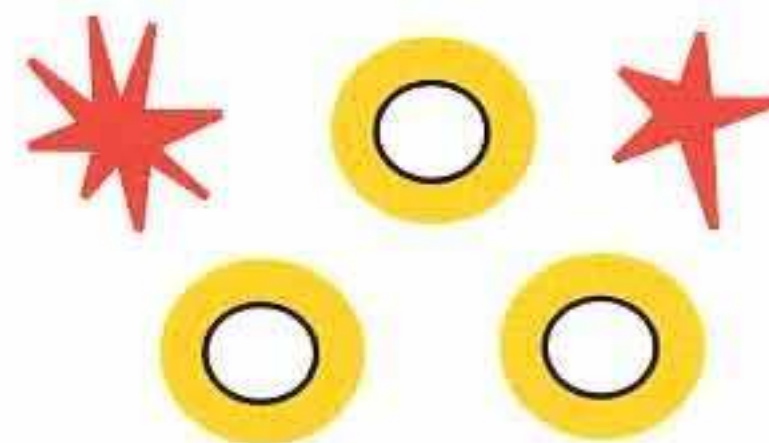
Technical information

HOW COMPLEMENT IS ACTIVATED



THE CLASSICAL PATHWAY

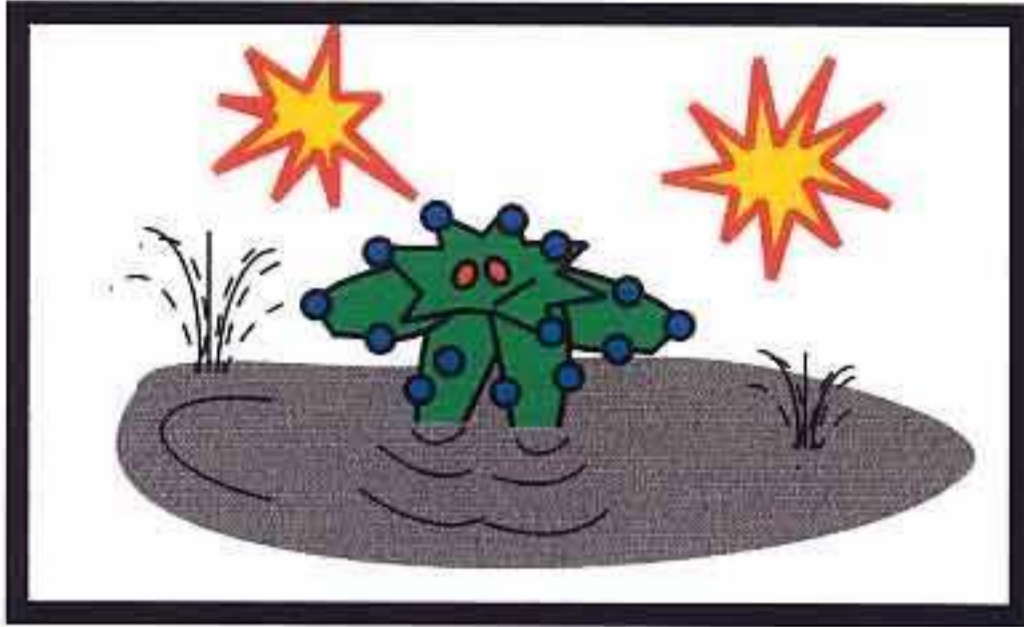
This involves IgG or IgM antibodies attaching onto something (see page 270).



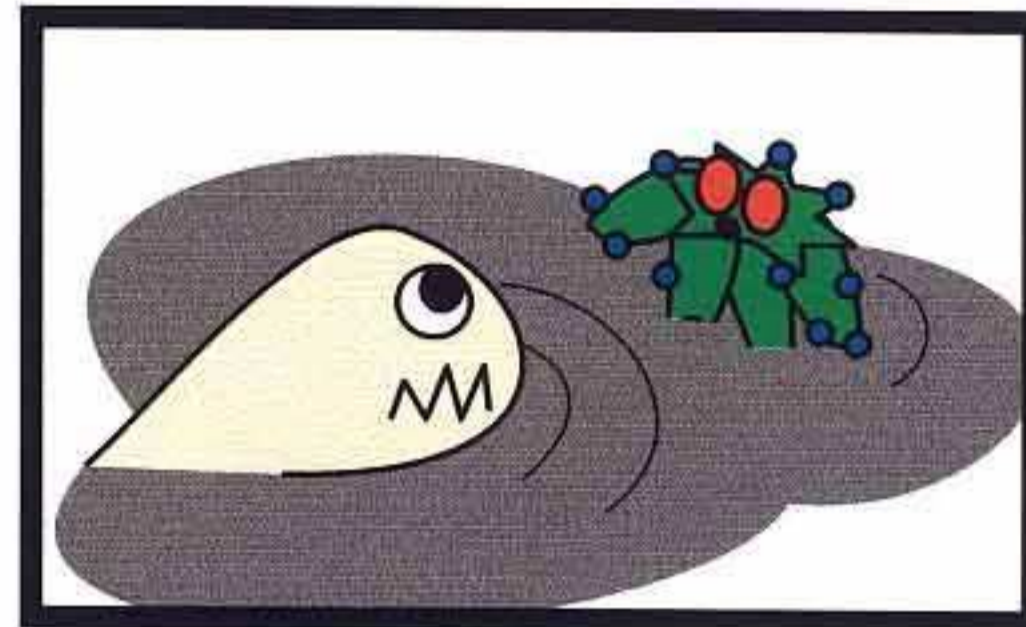
THE ALTERNATIVE PATHWAY

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

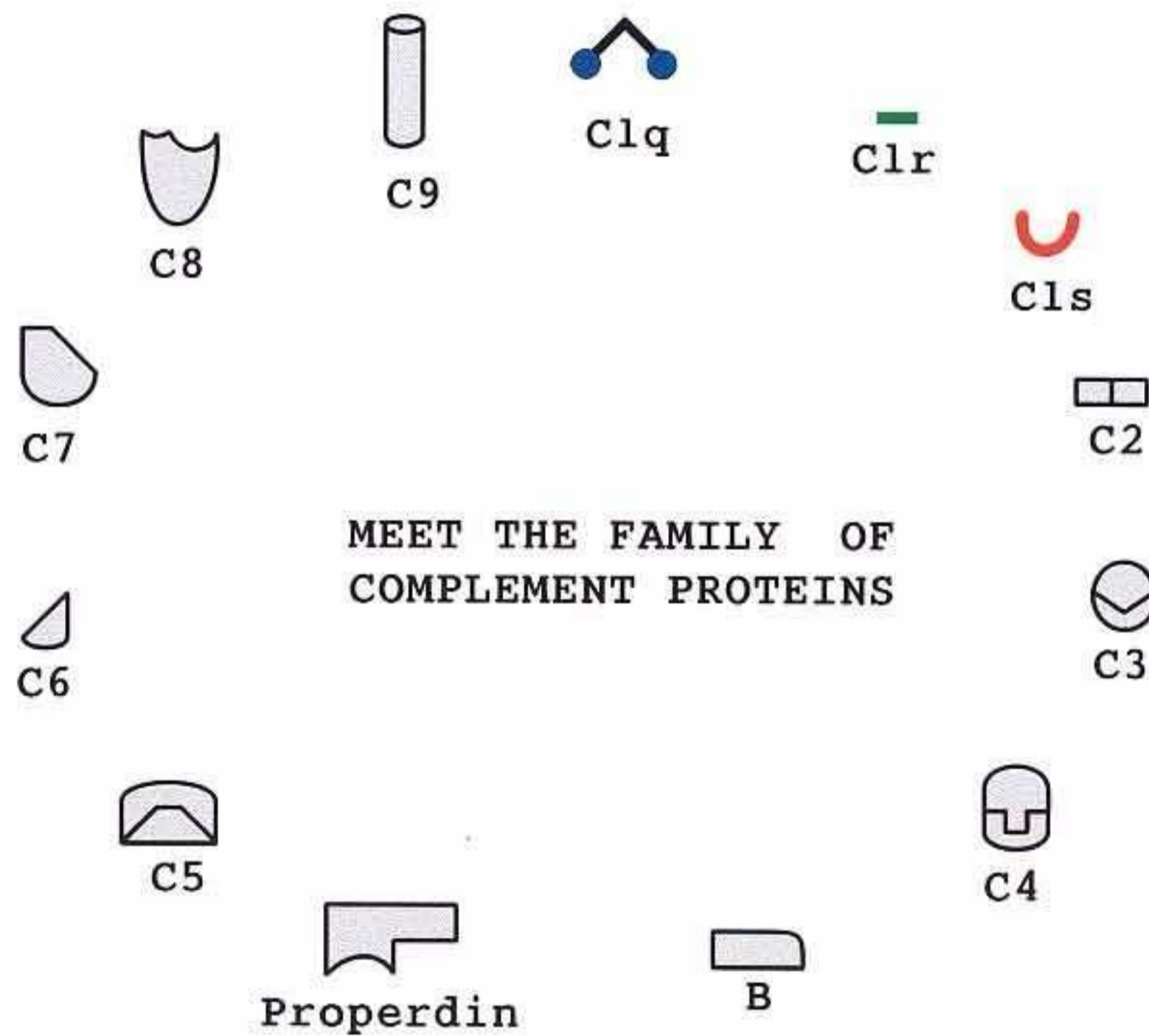
A MICROBE DROPS IN



Complement is quickly activated and coats the microbe.

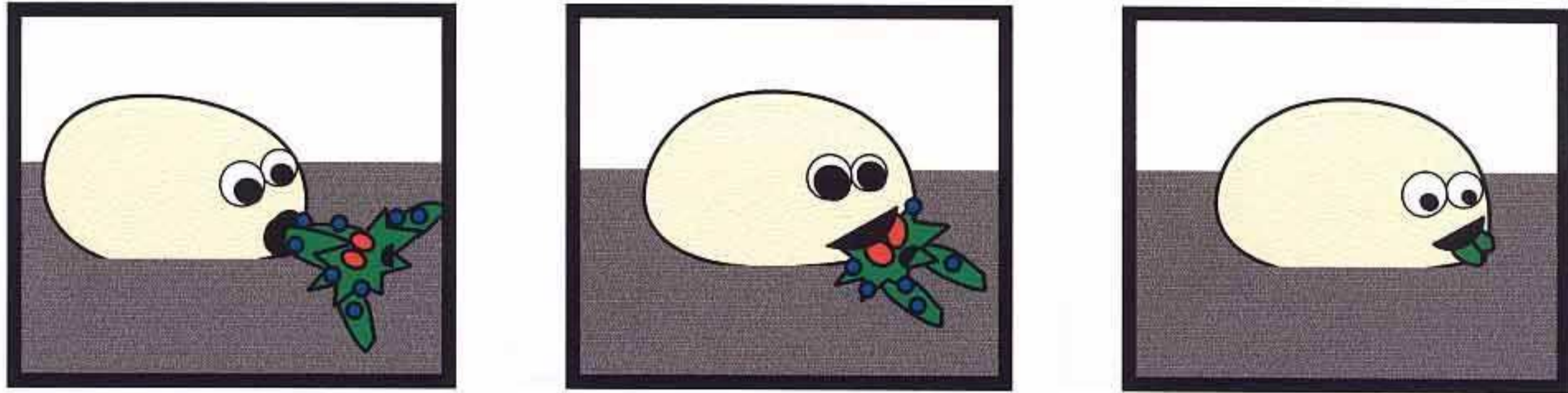


Then, like a creature from the deep, a neutrophil emerges.

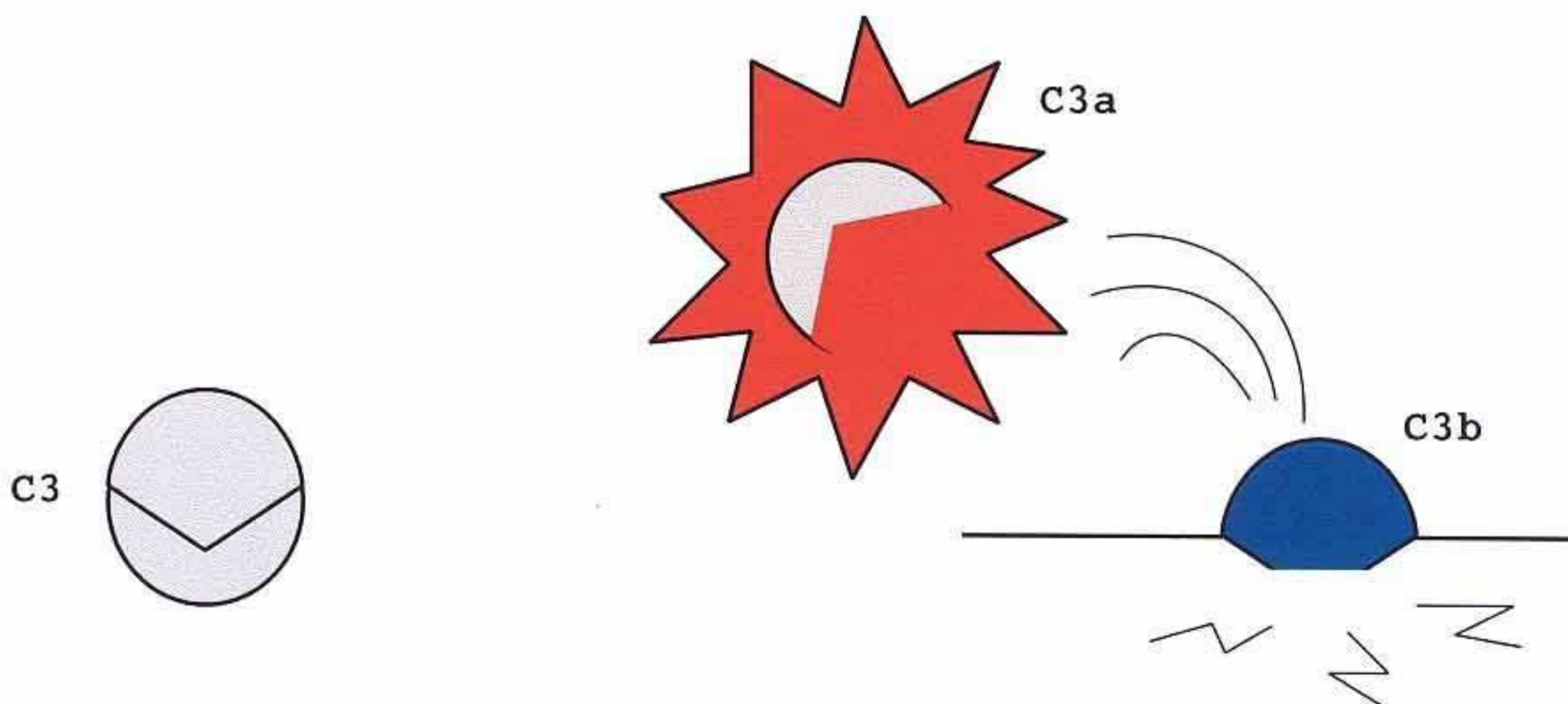


As complement is not one protein but many, they are sometimes referred to as the complement family. Found in blood in their inactive form, complement proteins are permanently damaged if heated above 56°C .

THE MICROBE IS QUICKLY GOBBLED UP



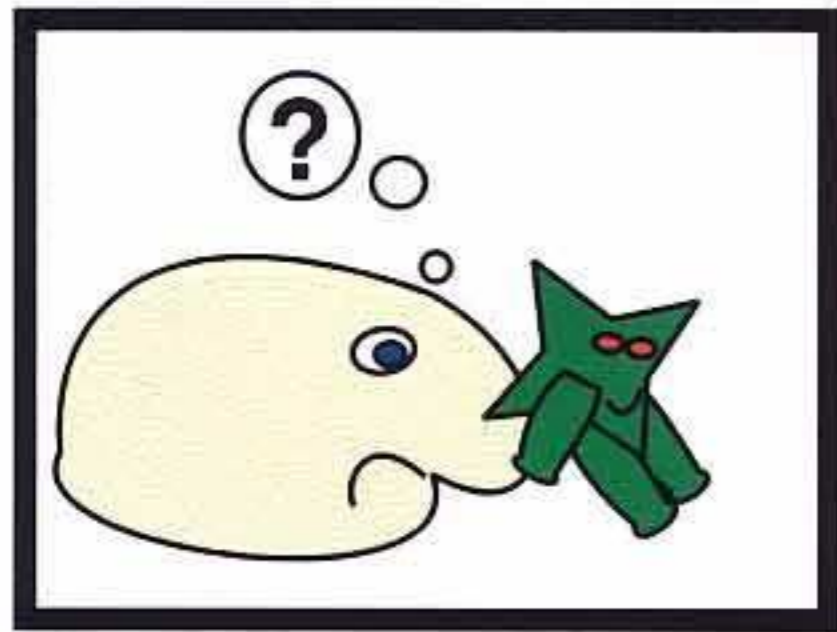
'Eating' this microbe is especially easy, as it is coated in complement C3b.



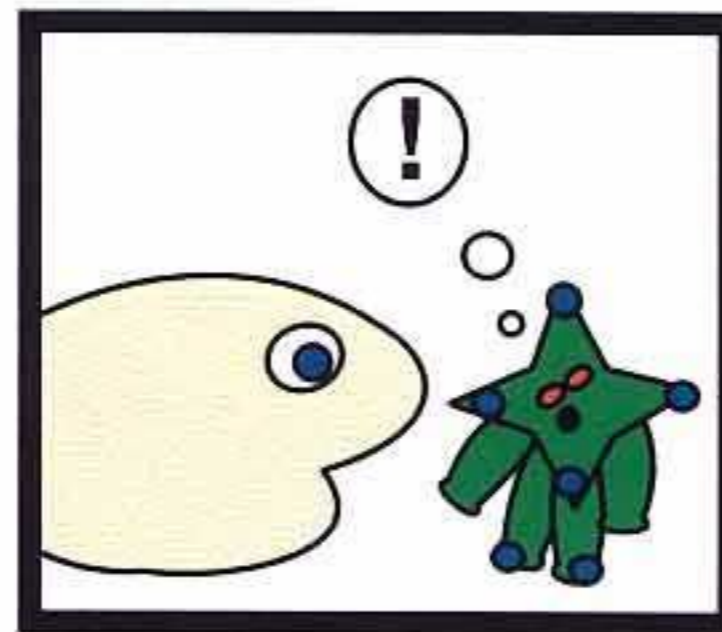
When complement C3 is activated, certain internal bonds are broken and it splits in 2.

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

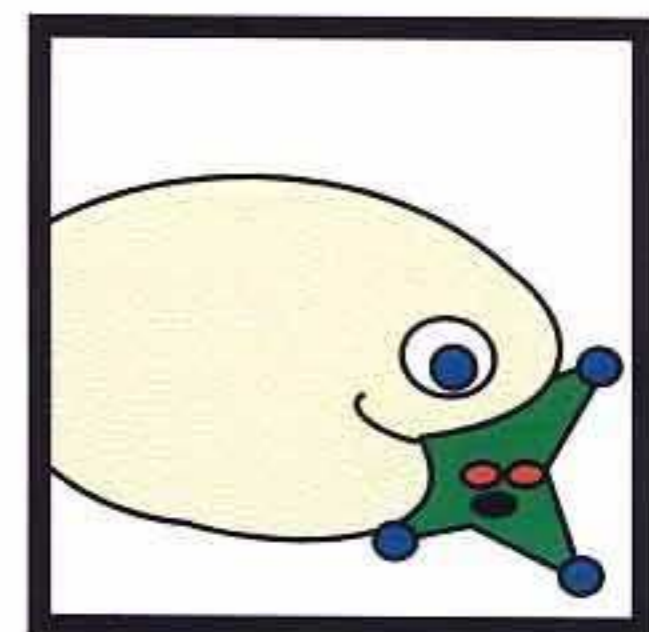
WHY IS IT EASIER TO 'EAT' THINGS COATED IN C3b?



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

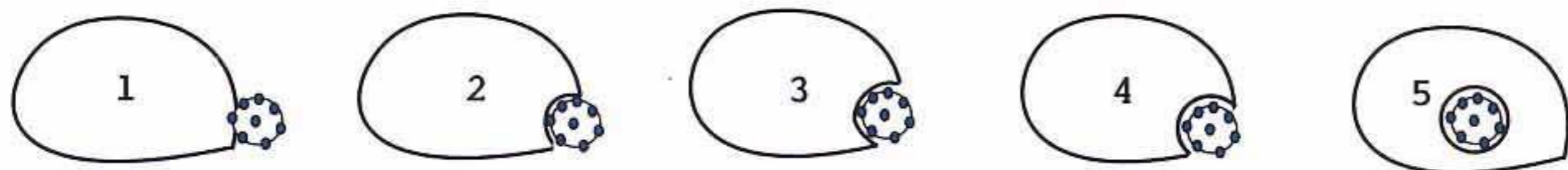


But usually it is not long before they are coated in complement C3b.



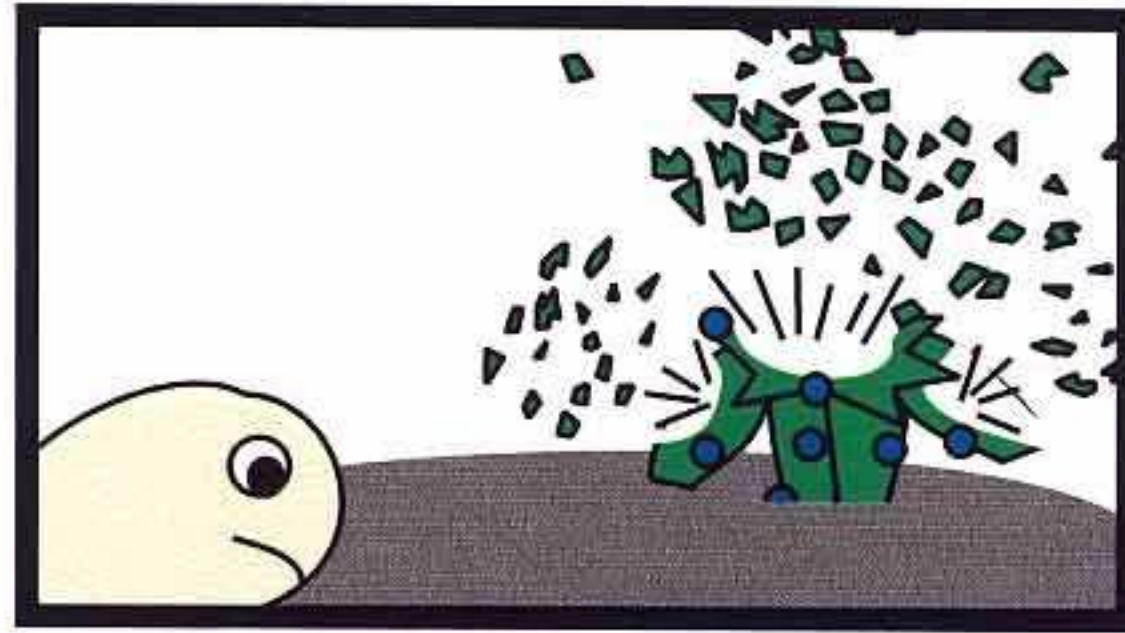
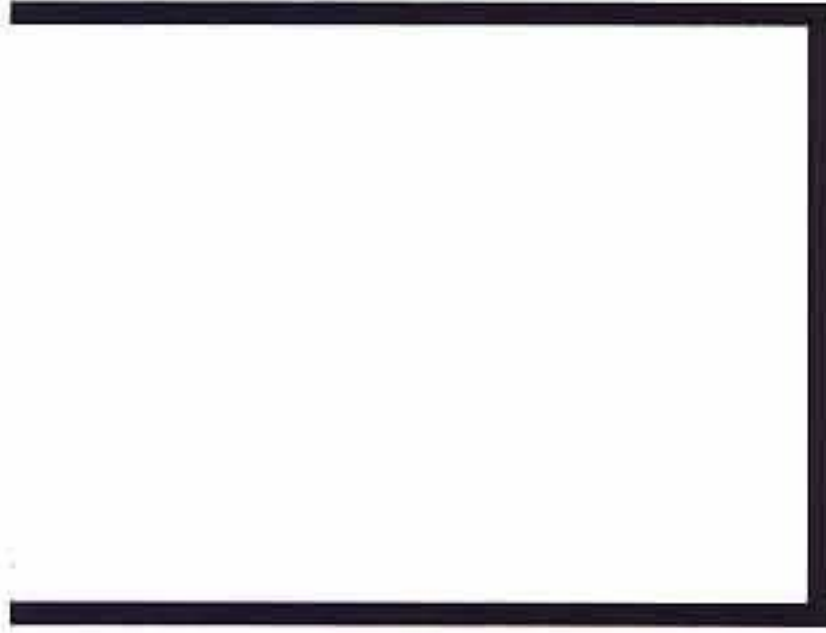
Now the immune cell can quickly 'gobble' up the bacteria.

PHAGOCYTOSIS

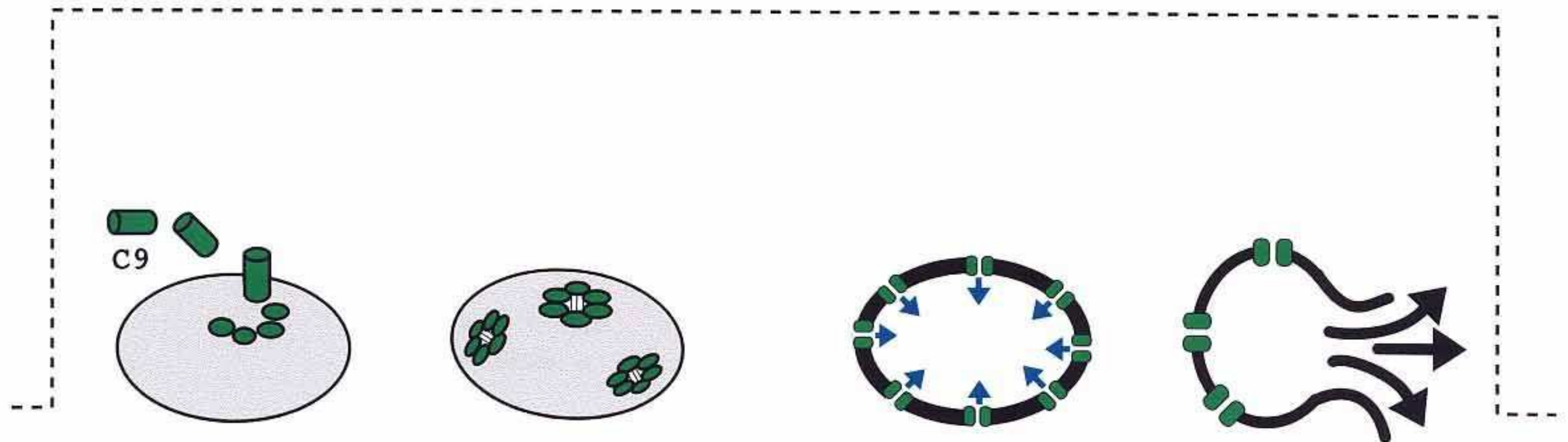


Macrophages and neutrophils have C3b surface receptors which 'lock' onto the C3b's that coat a microbe. This allows their membrane to envelop the microbe, like a zip being fastened.

THIS NEUTROPHIL ARRIVES TOO LATE!!!



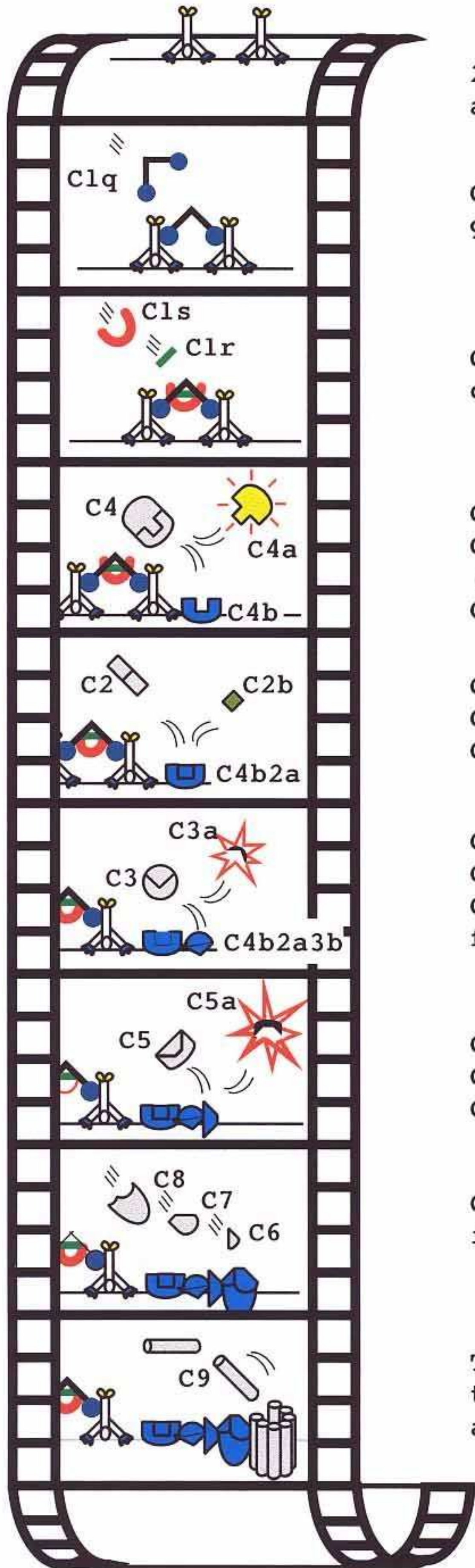
Just as he arrives, the microbe explodes.



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).

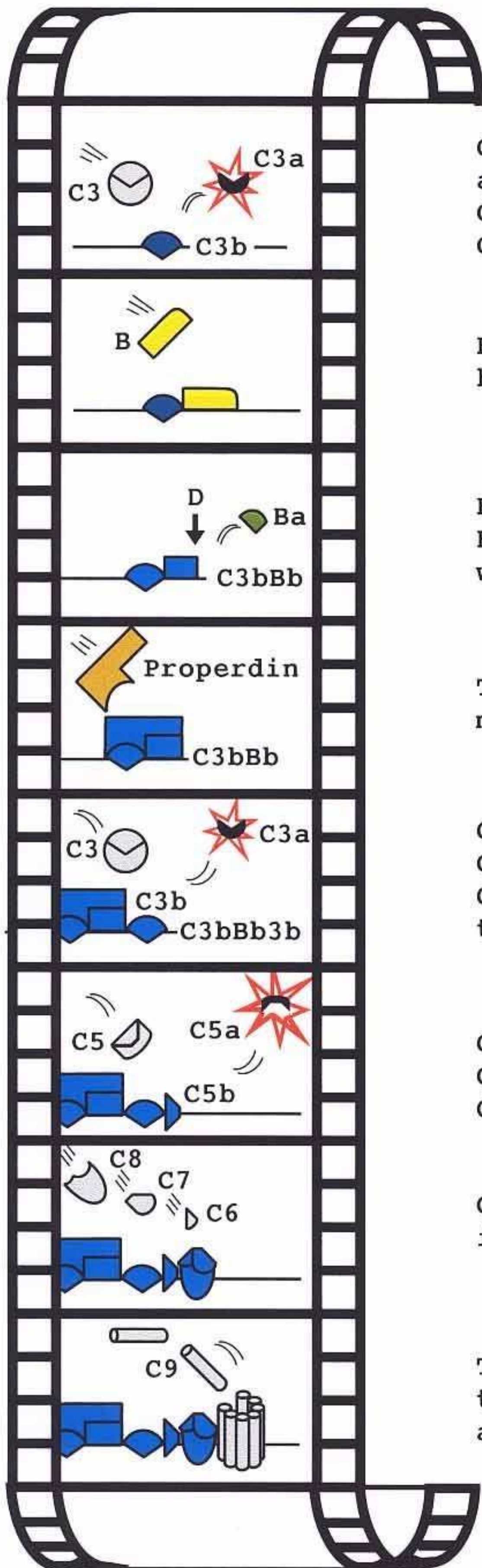
"THE FINAL COMMON PATHWAY"

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 stabilise C3 convertase.

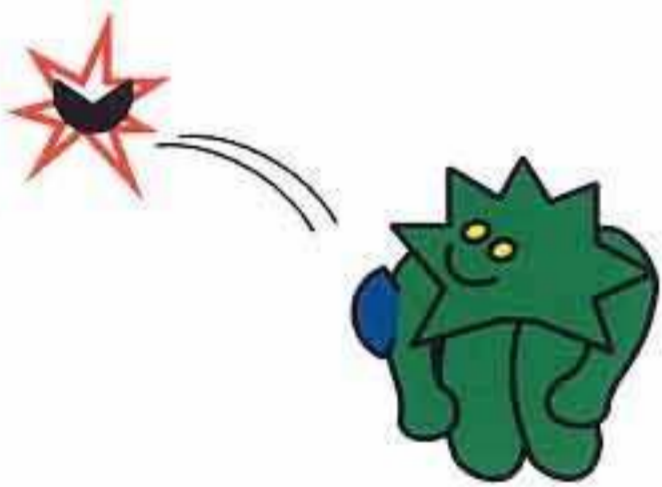
C3 convertase cleaves another C3. C3a goes off with a 'bang'. C3b attaches onto C3 convertase to form C5 convertase (C3bBb3b).

"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.