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PROTEINES À LA >UNE<

Issue 25, December 2008

About a tick

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Ticks are nasty. Carriers of disease and suckers of blood, they can turn a walk in the woods into a nightmare. Fortunately for us, there lies a brief truce in the winter when they burrow down into the earth for warmth. Mild Spring weather, however, brings them back to the surface where they wait patiently for an animal of some sort to sink their teeth into. Once firmly anchored, ticks are able to inject an arsenal of molecules into their host's system, which will help them cling more strongly, feed more freely and shun the host's immune system.

If you go down to the woods today…

Ticks are not insects. They have eight legs and belong to the same family as spiders – arachnids – which most of us find just as distasteful. Spiders make themselves at home almost anywhere but ticks only take up residence in forests. In Switzerland, they thrive all year round – though only exceptionally in the Winter – and in all parts of the country up to 1'500m altitude. Unlike what is commonly thought, ticks do not fall off trees; they are particularly fond of hedgerows and undergrowth, where they climb to the top of tall grasses and shrubs. There, they wait passively for a warm-blooded animal – a bird, a hedgehog, a deer, a dog or a human – to brush past them, when they'll seize the opportunity to hop onto them and suck their fill of blood.

… you're in for a big surprise…

This delightful state of affairs for a tick can be much less so for its host. It is precisely while feeding off us that a tick risks transmitting bacteria or viruses that could put our health in danger. Among the 800 species of ticks that exist, *Ixodes ricinus* gives the most concern in Europe because it is the carrier of two of the most dreaded pathogens: *Borrelia burgdorferi*, a bacterium, and a Flavivirus.

Borrelia burgdorferi causes Lyme disease, or borreliosis. In Switzerland, 2000 to 3000 people are infected every year. The first symptoms include inflammation where the skin has been punctured by the tick, followed by signs very similar to those we suffer from when down with the flu. The disease progresses by hitting the joints, the nervous system and more rarely the heart.

Flavivirus, on the other hand, is responsible for tick encephalitis which also starts off with flu-type symptoms which can develop into meningitis or inflammation of other parts of the brain. In Switzerland, the few ticks that are carriers of this virus thrive only in the northern cantons – which is why there are fewer cases of encephalitis than of Lyme disease (around 250 a year).

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Fig.1 *The* Ixodes ricinus tick. *There are three stages in its development: larva, nymph and finally adult.*

Lyme disease can be cured with antibiotics. And encephalitis can be avoided by vaccination. But better safe than sorry: the Swiss Federal Department of Health strongly recommends foresters, mushroom pickers, ramblers and joggers who live in exposed cantons to get vaccinated in the Winter so that they are protected at the start of the tick season – i.e. in April.

A discrete parasite

However efficient the vaccine against tick encephalitis may be, it does not prevent ticks from clinging to its host and injecting other viruses and bacteria. And the longer it clings the greater the risk of transmission. So how can we protect ourselves? To this day, no anti-tick vaccine has been found although researchers have been tackling the problem for years. The best protection is to prevent the ticks from settling. How? After a walk in the forest, inspect your clothes and body carefully. Ticks are tiny and very light; they can easily slip under your clothes where they look for parts of the skin which are tender such as the groin or neck, and behind the knees. Out of sight, they then sink their teeth into the flesh and remain there until sated.

If blood is unobtainable, ticks cannot continue their growth. Ticks are parasites and as such they help themselves according to their self-centred needs. At each stage of its development, a tick searches for a new host. The bigger it grows, the more it requires and a tick will suck blood for anything between two to ten days. Once satisfied, it becomes almost spherical and can reach one hundred times its original weight, by which time it falls to the ground. On the ground, it takes as long as it needs to digest the blood and begin its next stage of development or – if it's a female – lay millions of eggs (Fig.2).

The art of being invisible

If a tick goes unnoticed, it will suck its fill and then let go so discretely that no-one will be the wiser. This is because the bite of a tick causes neither irritation nor inflammation of the skin. And yet, it is

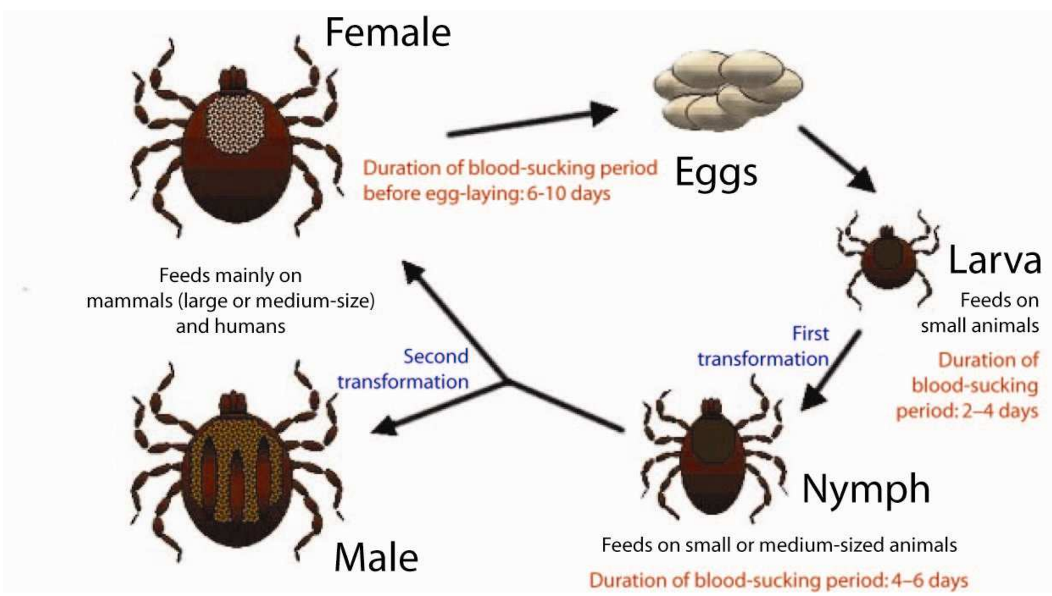

Fig.2 Ixodes ricinus' *life cycle*

frequently by scratching that we notice a tick's presence. Our immune system does not seem to detect it. Why not?

The answer is in the tick's saliva. To be able to suck blood, the tick punctures the skin of its host and introduces a sort of tube coated with bristles – called the rostrum (cf. Fig.3). The rostrum releases a powerful chemical cocktail composed of about 300 molecules, amongst which pain killers to lessen the sensation of the bite, anti-coagulants to thin the blood and, surprisingly, anti-inflammatory proteins that intercept any immune reaction.

Fig.3 *The "mouth" of* Ixodes ricinus*. Blood is sucked up through the rostrum, a tube-like structure coated with bristles. The rostrum has serrated edges which lacerate the host's skin when the tick is preparing to anchor.*

Researchers have recently brought to light a new family of proteins which they have named evasins. Evasins seem to be capable of interfering with the immune system. How? When ticks bite, the skin cells send off an alert signal by means of tiny proteins called chemokines. The role of chemokines is to attract immune cells to the site of intrusion, where they will get rid of a foreign body. The foreign body being – in this case – the tick. But the tick's evasins intercept the signal by binding to the chemokines, thereby neutralising them. Thus 'muzzled', the chemokines cannot give off their alert signal and an immune reaction is checked.

Evasins not only elude the immune system but also researchers. They are unlike any other known protein, although viral and other parasite proteins with anti-inflammatory properties have already been characterised. Scientists have nevertheless been able to establish that evasins are small and are able to recognize specifically certain chemokines. Evasins also have the unusual characteristic of carrying carbohydrate. Far from being purely decorative, carbohydrates put the immune system off its guard by concealing certain areas of the proteins that normally would give the alert as to the presence of an intruder. Consequently, evasins are double anti-inflammatory agents: not only do they block the host's immune reaction but the host itself is fooled.

Diverting evasins

Medical research is keen to understand how an immune reaction can be moderated. Indeed, many inflammatory diseases affecting the respiratory tract or the skin – such as asthma or allergies – as well as auto-immune diseases, like arthritis, are due to an immune system gone haywire. The object of several studies is to find substances which could moderate immune reactions and, consequently, calm inflammation. A few years ago, a first anti-inflammatory tick protein was characterised and researchers had high hopes. Alas… with no results. The discovery of evasins could inspire researchers to create a novel anti-inflammatory agent which would be both effective and have few side effects.

The muse of science

Nature is a limitless source of inspiration. Ticks are not the first blood-sucking parasites to have revealed extremely effective and enviable substances. These are creatures that have had millions of years to perfect their chemical know-how – ticks appeared well before the dinosaurs! Besides the coveted anti-inflammatory substances, blood-suckers have also evolved powerful anti-coagulants. Leeches were the first parasites ever to have served medicine and have now been reintroduced into microsurgery to prevent the formation of blood clots and to drain blood. Other anti-coagulant proteins from yet another parasite – the vampire bat – are under study for the treatment of heart attacks and strokes. The properties of vampire bat saliva were already deemed singular in the 1930s – possibly stimulated by the fascination of Count Dracula whose story was written towards the end of the 19th century and, besides filling the fantasies of millions of readers, inspired many a film-maker. Up to now however, vampire bats have only been known to attack cattle. Not humans…

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For further information

On the Internet:

- About ticks : http://en.wikipedia.org/wiki/Tick
- Lyme disease : http://en.wikipedia.org/wiki/Lyme_disease
- Tick encephalitis : http://en.wikipedia.org/wiki/Tick-borne_meningoencephalitis

Illustrations:

- Fig.1, Source : http://www.bag.admin.ch/themen/medizin/00682/00684/01069/index.html?lang=fr
- Fig.2, Adaptation : http://fr.wikipedia.org/wiki/Fichier:Image-Life_cycle_of_ticks_family_ixodidaeFr.jpg
- Fig.3, Source : http://www.bag.admin.ch/themen/medizin/00682/00684/01069/index.html?lang=fr

At UniProtKB/Swiss-Prot:

- Evasin-1, Rhipicephalus sanguineus (tick): P0C8E7
- Evasin-3, Rhipicephalus sanguineus (tick): P0C8E8
- Evasin-4, Rhipicephalus sanguineus (tick): P0C8E9

Date of French publication: December 18, 2008
Date of translation: February 25, 2009
