University of Salford MANCHESTER

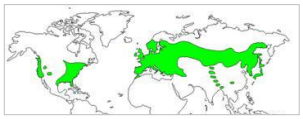
Something hungry is about to hatch

unravelling the natural transmission pathways of tick-borne pathogens in the UK

Richard Birtles
School of Environment & Life Sciences

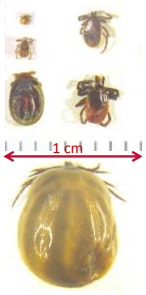
ticks in the UK, Europe & around the world

- ticks are second only to mosquitoes as vectors of pathogens of medical and veterinary importance.
- in UK, Europe and across the temperate northern hemisphere, ticks of the genus *Ixodes* are widespread and are vectors of numerous pathogens.



Ixodes species in the UK

- *Ixodes ricinus*, the sheep or deer tick, feeds on most mammals/birds, is widespread in the UK and is the most frequent biter of humans
- other *Ixodes* species also present in UK
  - *I. canisuga*
  - *I. hexagonus*
  - *I. trianguliceps*
  - these species have a far more limited host range and are far less frequently associated with humans.

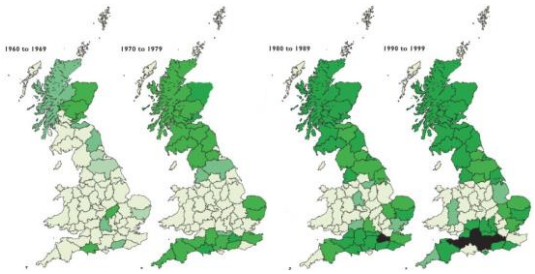


UK tick abundance is on the rise

- the distribution of *Ixodes ricinus* has expanded by 17% in comparison with the previously known distribution.
- people perceive there to be more ticks today than in the past at 73% of locations studied.
- reported increases in tick numbers coincided spatially with perceived increases in deer numbers.

Scharlemann *et al.* Med Vet Entomol 2008;22:238-47.

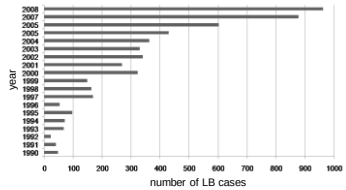
UK tick abundance is on the rise



Roe deer bag density (number shot per 100 hectares) synoptically by county and by decade from 1960 to 1999. Source: Game & Wildlife Conservation Trust

UK tick abundance is on the rise

England & Wales (HPA)

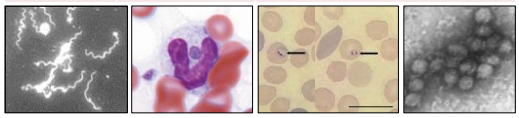


Scotland (HPS)

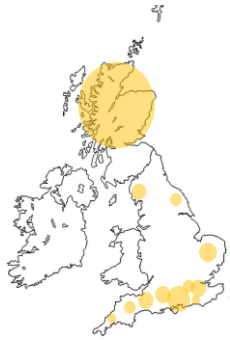
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Borrelia (total) (Lyme Disease)[1]	37	28	85	81	86	96	171	230	285	605
Borrelia burgdorferi	37	28	63	71	86	96	171	230	285	605
Borrelia species	0	0	22	10	0	0	0	0	0	0

established tick-borne pathogens in the UK

agent	disease	medical/veterinary relevance in UK
Borrelia burgdorferi	lyme borreliosis	1500+ human cases p.a. - disease also reported in companion animals & horses.
Anaplasma phagocytophilum	granulocytic anaplasmosis, pasture fever, tick pyaemia	pathogen of young sheep, also reported in companion animals & horses – 1 human case. c1,000 human cases p.a. in US.
Babesia spp.	babesiosis	*B. divergens* causes redwater fever in cattle. *B. microti* is an emerging zoonotic pathogen in US.
louping ill virus	louping ill	pathogen of young sheep - close relative of tick-borne encephalitis virus.



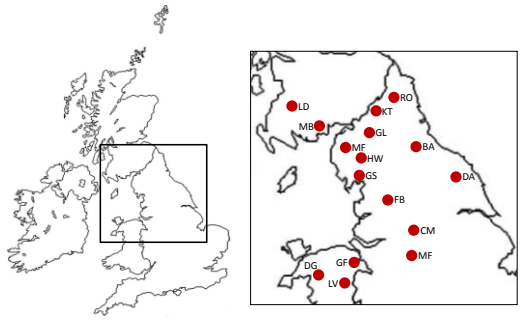
UK "hot-spots" of Lyme borreliosis



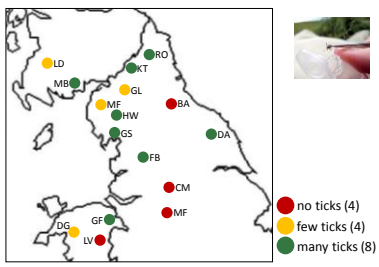
"where there are ticks, there's Lyme"

how much variation is there in *B. burgdorferi* infection prevalence in geographically-distinct *I. ricinus* populations?

central UK study area: 16 study sites

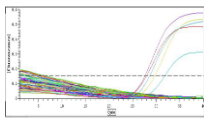


encounter with ticks



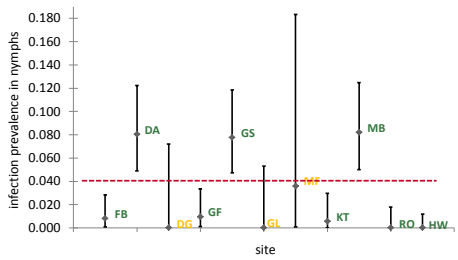
detecting *B. burgdorferi* DNA in ticks

DNA extracts prepared from *I. ricinus* and incorporated in *B. burgdorferi s.l.*-specific real-time PCR targeting a 23S rDNA fragment.

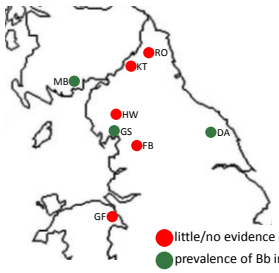


site	code	adults	nymphs
Forest of Bowland	FB	2/14	2/251 (<1%)
Dalby Forest	DA	2/20	19/237 (8%)
Dolgellau Forest	DG	0/2	0/40 (0%)
Graigfechan	GF	0/22	2/212 (<1%)
Grange-over-Sands	GS	6/29	19/245 (8%)
Gilsland	GL	0/16	0/55 (0%)
Keswick	MF	0/2	1/28 (4%)
Kielder Water	KT	0/100	1/185 (<1%)
Loch Doon	LD	0/0	0/12 (0%)
Mabie Forest	MB	0/18	19/232 (8%)
Rothbury Forest	RO	0/6	0/167 (0%)
Haweswater	HW	0/72	0/249 (0%)

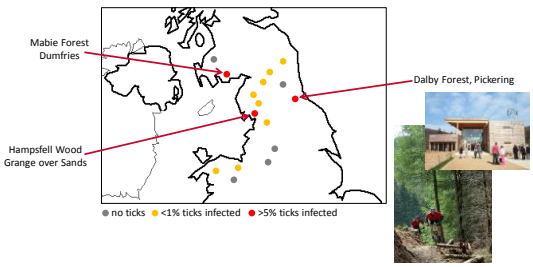
B. burgdorferi infection prevalence



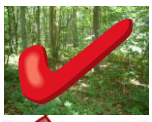
geographical distribution of infected ticks



outdoor activity at high prevalence sites



association with habitat

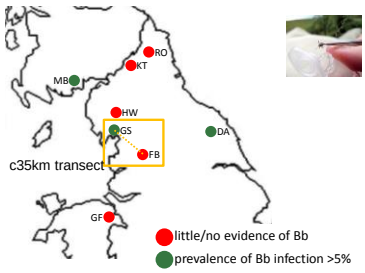


deciduous/mixed woodland (3 sites)

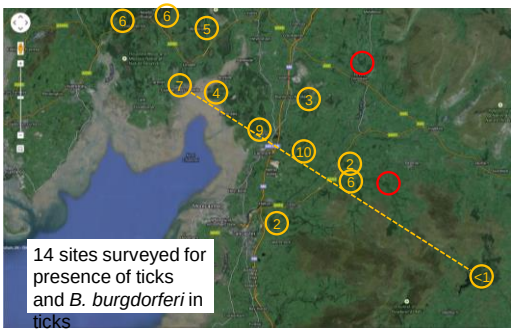
conifer plantation/grassland (3 sites)

bracken/moorland (2 sites)

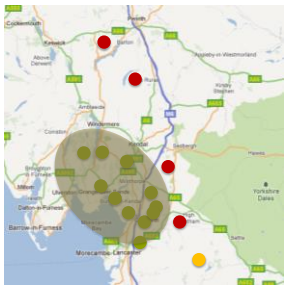
clarifying “hotspots”



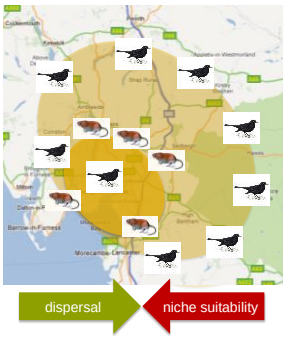
clarifying “hotspots”



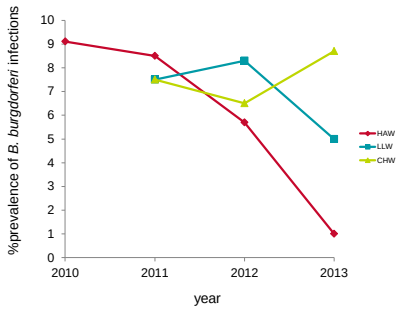
clarifying "hotspots"



clarifying "hotspots"



B. burgdorferi infection prevalence

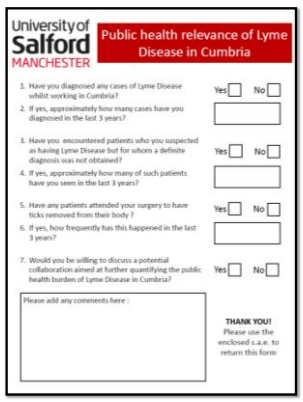


summary 1

- some supposedly "ticky" places lacked ticks.
- the prevalence of *Bb* in "ticky" places varied significantly.
- there was more *Bb* in ticks living in deciduous woodland than in ticks living in other habitats.
- the prevalence of *Bb* at specific sites varied from year to year, sometimes dramatically; the relative abundance of specific *Borrelia* genospecies also varied from year to year, sometimes dramatically.
- we don't really know the determinants of these dynamics – and as the number of cases of LB in the UK rises, there is an increasing need for a better understanding of them.

how common really is Lyme borreliosis?

- all this ecology is well and good, but we wanted a way to engage with local health practitioners across our study area with the aim of getting a handle on the perceived importance of LB in the area.
- we decided to send them a questionnaire…


University of Salford MANCHESTER

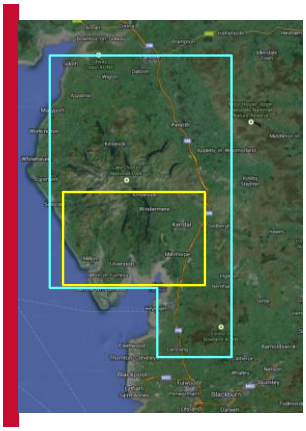
Public health relevance of Lyme Disease in Cumbria

1. Have you diagnosed any cases of Lyme Disease whilst working in Cumbria? Yes ☐ No ☐
2. If yes, approximately how many cases have you diagnosed in the last 3 years?
3. Have you encountered patients who you suspected as having Lyme Disease but for whom a definite diagnosis was not obtained? Yes ☐ No ☐
4. If yes, approximately how many of such patients have you seen in the last 3 years?
5. Have any patients attended your surgery to have ticks removed from their body ? Yes ☐ No ☐
6. If yes, how frequently has this happened in the last 3 years?
7. Would you be willing to discuss a potential collaboration aimed at further quantifying the public health burden of Lyme Disease in Cumbria? Yes ☐ No ☐

Please add any comments here :

THANK YOU!
Please use the enclosed s.a.e. to return this form

- 67 GPs in 20 practices (including some in northern Lancashire) approached
- 40/67 responded, representing 18/20 practices
- 21 responders had seen at least 1 LB case in last 3 yrs (range: 1-10) and 21 responders had seen at least 1 case of suspected but unproven LB in the last 3 yrs.
- GPs at 16/18 practices had removed ticks from at least 1 patient in the last 3 yrs, more than half of GPs doing this over 10 times



In total, the 21 responders reported 59 confirmed and 84 suspected cases of LB.

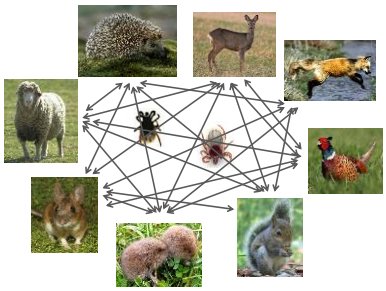
These responders care for a total of about 46,000 patients.

Epidemiologists at Public Health England have recorded only 51 cases of LB in the whole of Northwest England in the past 35 years.

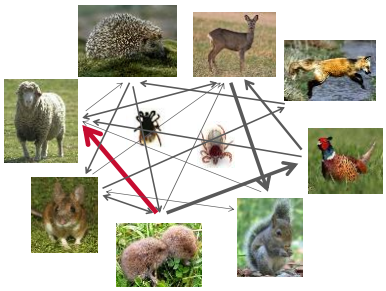
A. phagocyophilum

- intracellular bacterium that parasitizes neutrophils.
- threatens livestock (pasture fever) in N Europe and humans (granulocytic anaplasmosis) in Europe, Asia & N America.
- when symptomatic, presents as an acute febrile syndrome with history of lethargy and anorexia. AP-mediated immuno-modulation provokes secondary infections (tick pyaemia).
- "generalist" species, exploiting a wide range of mammals and multiple species of ixodid ticks.
- first confirmed human case in UK reported earlier this year – numerous cases reported in mainland Europe and thousands in US.

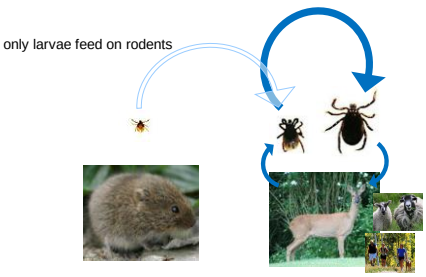
complex transmission network of a "generalist" parasite



complex transmission network of a "generalist" parasite

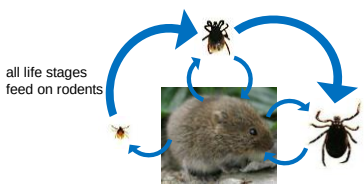


AP transmission in an *I. ricinus* system



trans-stadial but <u>not</u> trans-ovarial transmission, thus rodents cannot serve as a source of infection to larval ticks

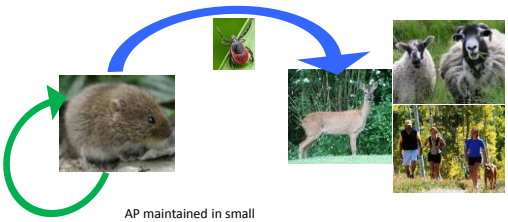
AP transmission in an *I. trianguliceps* system



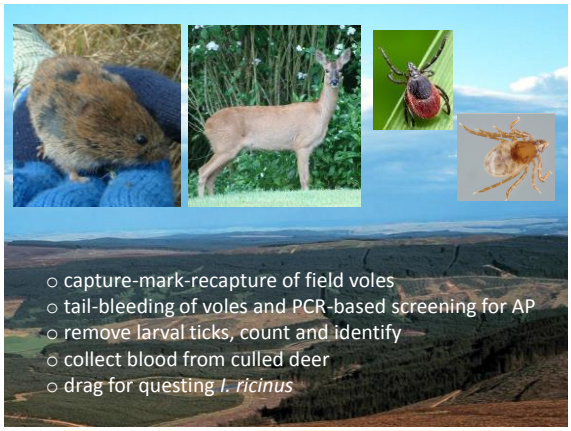
trans-stadial but <u>not</u> trans-ovarial transmission, but rodents do serve as a source of infection to larval ticks

AP transmission in an multi-vector system: a hypothesis

I. ricinus larvae act as a bridging vector, transmitting AP from small mammals to other hosts



AP maintained in small mammals by *I. trianguliceps*

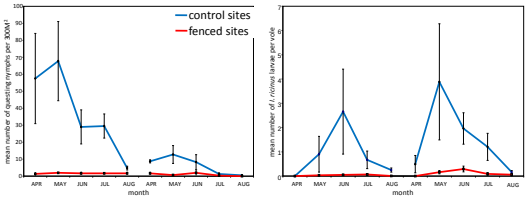


- capture-mark-recapture of field voles
- tail-bleeding of voles and PCR-based screening for AP
- remove larval ticks, count and identify
- collect blood from culled deer
- drag for questing *I. ricinus*

assessing the relative contributions of *I. ricinus* and *I. trianguliceps* to AP maintenance in voles

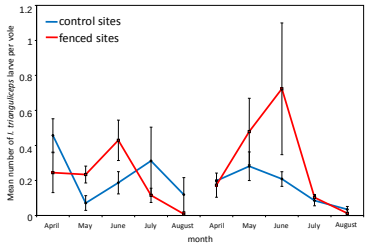
comparison of AP infection dynamics in vole populations with and without the presence of *I. ricinus*.

assessing the relative contributions of *I. ricinus* and *I. trianguliceps* to AP maintenance in voles



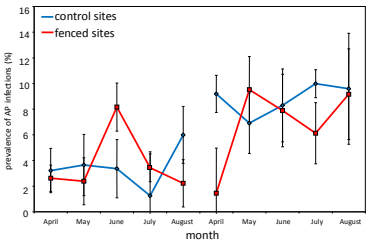
questing *I. ricinus* were virtually absent from the deer exclosures

assessing the relative contributions of *I. ricinus* and *I. trianguliceps* to AP maintenance in voles



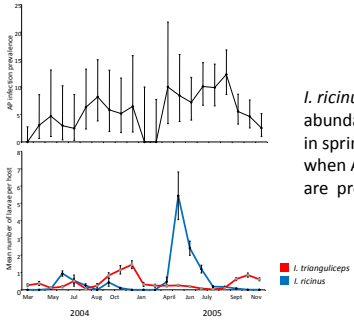
the existence of deer exclosures makes no significant difference to the numbers of *I. trianguliceps* larvae on voles

assessing the relative contributions of *I. ricinus* and *I. trianguliceps* to AP maintenance in voles



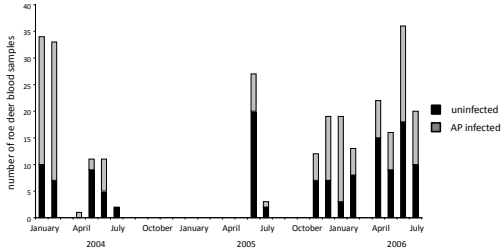
AP infection prevalence not significantly different between vole populations inside or outside deer exclosures

I. ricinus larvae infest AP-infected rodents



I. ricinus larvae are abundant on voles in spring & summer when AP infections are prevalent

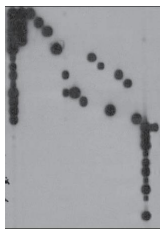
AP is transmitted by *I. ricinus*



AP infections are highly prevalent in roe deer, peaking at about 70% during the summer months

quantifying the bridging role of *I. ricinus* larvae

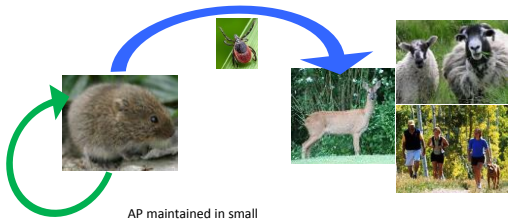
30/4984 (0.7%) of questing *I. ricinus* nymphs infected with AP.



PCR-based detection of bloodmeal remnants in questing *I. ricinus* nymphs revealed that 65% fed on field voles as larvae, compared to <15% for other hosts, hence field voles are by far the most important host for *I. ricinus* larvae…

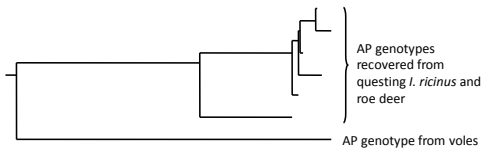
AP transmission in an multi-vector system: a hypothesis

I. ricinus larvae act as a bridging vector, transmitting AP from small mammals to other hosts



AP maintained in small mammals by *I. trianguliceps*

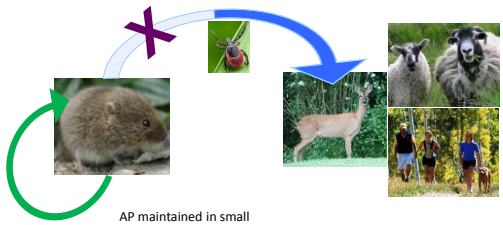
genotyping of AP strains infecting different hosts and vectors



the vole-associated AP sequence type was divergent from those encountered in *I. ricinus* and in roe deer

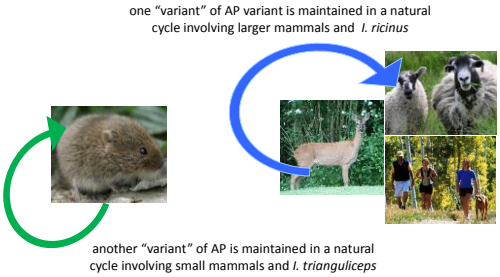
AP transmission in an multi-vector system: hypothesis rejected

I. ricinus larvae act as a bridging vector, transmitting AP from small mammals to other hosts



AP maintained in small mammals by *I. trianguliceps*

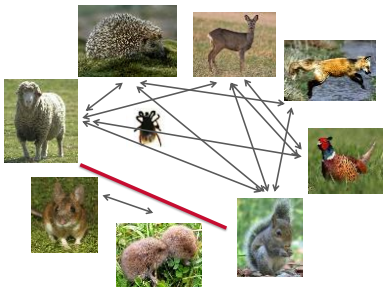
AP transmission in an multi-vector system: discrete but co-existing transmission cycles



AP transmission in an multi-vector system: consequences

1. the vole-associated AP genotype is restricted to a small rodent/*I. trianguliceps* cycle, hence is not of veterinary/public health concern.
2. discrete co-existing transmission cycles can be associated with dilution of abundance of tick-borne pathogens when, at first sight, an augmentation would be the expected outcome.

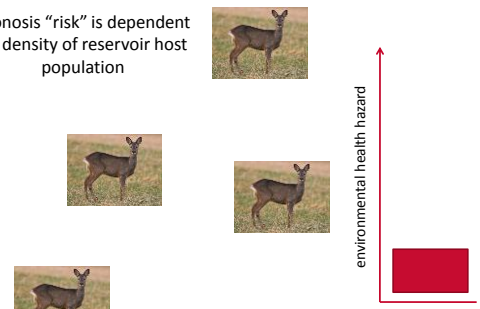
complex transmission network of a "generalist" parasite

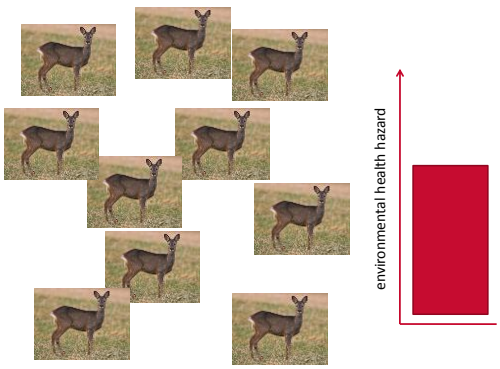


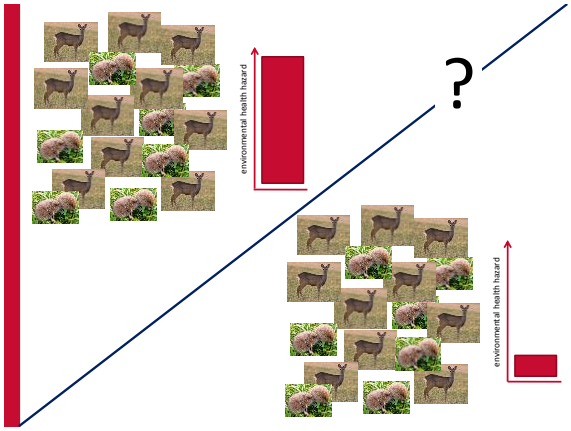
AP transmission in an multi-vector system: consequences

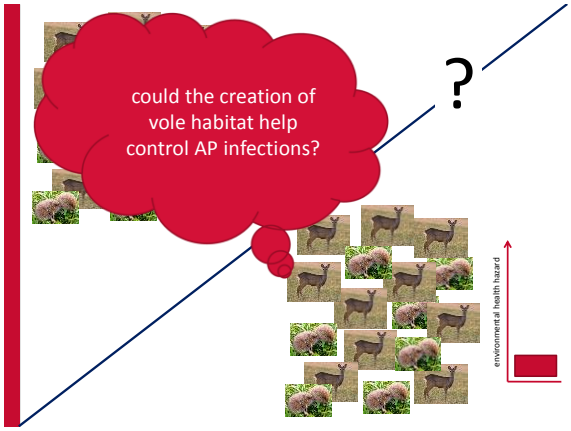
1. the vole-associated AP genotype is restricted to a small rodent/*I. trianguliceps* cycle, hence is not of veterinary/public health concern.
2. discrete co-existing transmission cycles can be associated with dilution of abundance of tick-borne pathogens when, at first sight, an augmentation would be the expected outcome.

zoonosis "risk" is dependent on density of reservoir host population



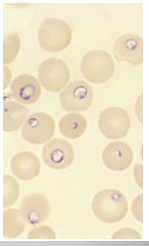






B. microti

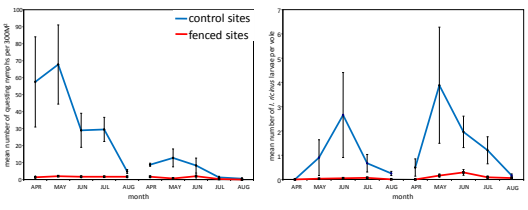
- protozoan apicomplexan parasite
- parasitizes erythrocytes
- holarctic small mammals serve as its animal reservoir
- human infection can be severe, particularly in the immuno-compromised, with malaria-like symptoms (cycling fever, chills, headache), anaemia, jaundice and blood in the urine.



assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles

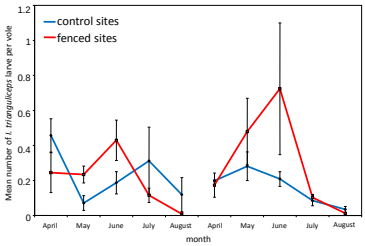
comparison of *B. microti* infection dynamics in vole populations with and without the presence of *I. ricinus*.

assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles



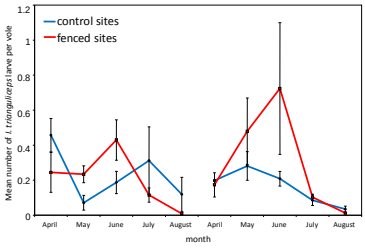
questing *I. ricinus* were virtually absent from the deer exclosures

assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles



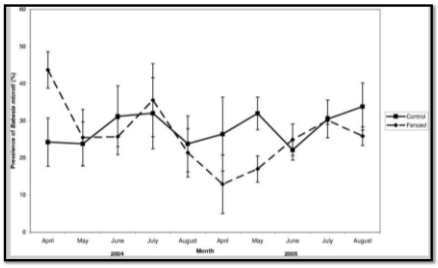
the existence of deer exclosures makes no significant difference to the numbers of *I. trianguliceps* larvae on voles

assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles



the existence of deer exclosures makes no significant difference to the numbers of *I. trianguliceps* larvae on voles

assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles



B. microti infection prevalence not significantly different between vole populations inside or outside deer exclosures.

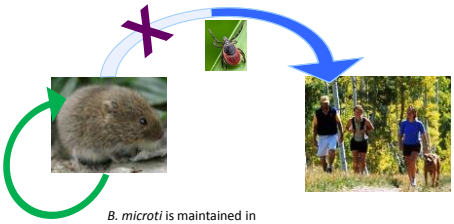
assessing the relative contributions of *I. ricinus* & *I. trianguliceps* to *B. microti* maintenance in voles

- no evidence of *B. microti* infections in (over 1000 tested so far) questing *I. ricinus.*
- no evidence of *B. microti* infections in deer.
- thus, our data support the previously proposed and tested hypothesis that *B. microti* is exploits small mammals as reservoir hosts, between which it is transmitted solely by *I. trianguliceps*.
- as *I. trianguliceps* does not bite humans, *B. microti* is unlikely to be a public health threat in the UK.


Quantifying parameters in the transmission of *Babesia microti* by the tick *Ixodes trianguliceps* amongst voles (*Clethrionomys glareolus*)

B. microti is "trapped" in an enzootic cycle, isolated from humans

I. ricinus is not competent vector for *B. microti* so cannot act as a bridging vector, transmitting the protozoa to humans.



B. microti is maintained in small mammals by *I. trianguliceps*

thanks

Kevin Bown, Gill Telford, Gill Hutchinson, Judy Bettridge, Marine Renard, Tong Zhao, Chris Ball, Natalie McConville, Lauren Perrin, Sandra Telfer, Nick Ogden, Xavier Lambin, Mike Begon, The Forestry Commission, DEFRA VTRI, The Wellcome Trust and The Henry Lester Trust.