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1 **An endemic hantavirus in field voles in northern England**

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7 **Article summary line:** Data are presented establishing the endemicity in northern England
8 of the Tatenale hantavirus lineage.

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10 **Running title:** An endemic hantavirus in U.K. field voles.

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22 Abstract

23 We report a PCR survey of hantavirus infection in the extensive field vole (*Microtus agrestis*)
24 populations occurring in the Kielder Forest, northern England. A Tatenale virus-like lineage
25 was frequently detected (~ 15% prevalence) in liver tissue. Such lineages are likely to be
26 endemic in northern England.

27

28 Recently a new vole-associated hantavirus (Tatenale virus) was discovered in northern
29 England (1), but only from a single individual of the field vole, *Microtus agrestis*. This finding
30 was particularly notable as only hantaviruses from murine-associated lineages (Seoul virus,
31 SEOV and SEOV-like viruses) had previously been reported in the U.K., despite the
32 abundance of potential vole hosts in the mainland U.K. and the endemicity of vole-
33 associated lineages (Puumala virus (PUUV) and Tula virus (TULV)) in mainland Europe (2).
34 Here we present data establishing the endemicity in northern England of the Tatenale virus
35 lineage.

36 European hantaviruses are of public health significance as a causative agent of
37 haemorrhagic fever with renal syndrome (HFRS). In the U.K., HFRS cases have primarily
38 been attributed to SEOV-like viruses on the basis of serological tests. Anti-SEOV antibodies
39 have been detected in both humans and Norway rats (*Rattus norvegicus*) in Northern Ireland
40 and Yorkshire (3, 4), seropositivity in humans correlating with domestic or occupational
41 exposure to rats (3, 5). However, there have been U.K. cases of HFRS with serological
42 cross reactivity to PUUV (3) which may share antigenic determinants with Tatenale virus.

43 To investigate the endemicity of hantavirus in U.K. field voles, we surveyed the extensive
44 populations of this species occurring in the Kielder Forest, Northumberland (~230 Km distant
45 from the locality where Tatenale virus was discovered). All sampled sites were grassy clear-
46 cut areas (adjacent to forest stands) where field voles are the dominant component of rodent
47 assemblages. Fieldwork was approved by the University of Liverpool Animal Welfare Ethical
48 Review Board and conducted subject to U.K. Home Office project licence PPL 70_8210.

49 Following the capture and processing of animals as previously described (6), viral RNA was
50 extracted from 48 livers using a QIAamp Viral RNA Mini Kit (Qiagen, U.K.) and converted to
51 cDNA using a High-Capacity RNA-to-cDNA Kit (Applied Biosystems, ThermoFisher
52 Scientific, U.K.). Detection of hantaviruses was, following Klempa *et al.* (2006) (7), carried
53 out by PCR amplification of a fragment of the genomic L segment encoding RNA-
54 polymerase.

55 PCR positives were recorded for 14.6% of voles (7/48), at 3 of 5 sampled sites (Figure,
56 panel A) and across the full survey period (March to September 2015). Three positive
57 samples from different individuals were sequenced (in both directions from independent
58 replicate PCR reactions) by Sanger sequencing (Source BioScience, U.K.). A 380bp
59 sequence was determined (GenBank accession numbers: KY751731, KY751732) in all three
60 positive vole samples, with a single nucleotide polymorphism at position 145 (adenine, 2
61 individuals; guanine, 1 individual). Whilst the recovered sequences were close to Tatenale
62 virus, there was significant divergence from this (respectively 86.0-86.3% and 95.9-96.7%
63 identity at the nucleotide and amino acid level) (Technical appendix). Phylogenetic analysis
64 (Figure, panel B) of the L segment demonstrated this level of divergence was comparable to
65 the divergence amongst many western European lineages of PUUV.

66 Taken together with the original record these data are sufficient to suggest that Tatenale-like
67 hantavirus lineages are widespread and locally common in northern England. Furthermore,
68 the considerable sequence divergence between samples in Cheshire and Northumberland is
69 consistent with long-standing endemicity in northern England. Given that PUUV has never
70 been recorded in the U.K.(2, 8), the possibility should be considered that a Tatenale-like
71 virus could be responsible for some U.K. HFRS cases. More studies are now needed to
72 confirm the status of other common U.K. rodents as hosts for this virus, and to further
73 characterize its phyletic relationships and zoonotic potential. Importantly, the cross-reactivity
74 of Tatenale-like virus infected sera to antigens from other relevant hantaviruses should be
75 determined to inform future serological surveys and the diagnosis of human HFRS cases.

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80 **References**

- 81 1. Pounder KC, Begon M, Sironen T, Henttonen H, Watts PC, Voutilainen L, et al. Novel
82 hantavirus in wildlife, United Kingdom. *Emerg Infect Dis.* 2013;19:673.
- 83 2. Bennett E, Clement J, Sansom P, Hall I, Leach S, Medlock JM. Environmental and
84 ecological potential for enzootic cycles of Puumala hantavirus in Great Britain. *Epidemiol
85 Infect.* 2010;138:91-8.
- 86 3. Jameson LJ, Newton A, Coole L, Newman EN, Carroll MW, Beeching NJ, et al.
87 Prevalence of antibodies against hantaviruses in serum and saliva of adults living or working
88 on farms in Yorkshire, United Kingdom. *Viruses.* 2014;6:524-34.

- 89 4. McKenna P, Clement J, Matthys P, Coyle PV, McCaughey C. Serological evidence of
90 Hantavirus disease in Northern Ireland. *J Med Virol.* 1994;43:33-8.
- 91 5. Jameson LJ, Taori SK, Atkinson B, Levick P, Featherstone CA, van der Burgt G, et
92 al. Pet rats as a source of hantavirus in England and Wales, 2013. *Euro Surveill.* 2013;18.
- 93 6. Jackson JA, Begon M, Birtles R, Paterson S, Friberg IM, Hall A, et al. The analysis of
94 immunological profiles in wild animals: a case study on immunodynamics in the field vole,
95 *Microtus agrestis*. *Mol Ecol.* 2011;20:893-909.
- 96 7. Klempa B, Fichet-Calvet E, Lecompte E, Auste B, Aniskin V, Meisel H, et al.
97 Hantavirus in African wood mouse, Guinea. *Emerg Infect Dis.* 2006;12:838-40.
- 98 8. Pether JV, Lloyd G. The clinical spectrum of human hantavirus infection in Somerset,
99 UK. *Epidemiol Infect.* 1993;111:171-5.
- 100 9. Ronquist F, Huelsenbeck JP. MrBayes 3: Bayesian phylogenetic inference under
101 mixed models. *Bioinformatics.* 2003;19:1572-4.
- 102 10. Nylander J. MrModeltest v2. Program distributed by the author. Evolutionary Biology
103 Centre, Uppsala University; 2004.

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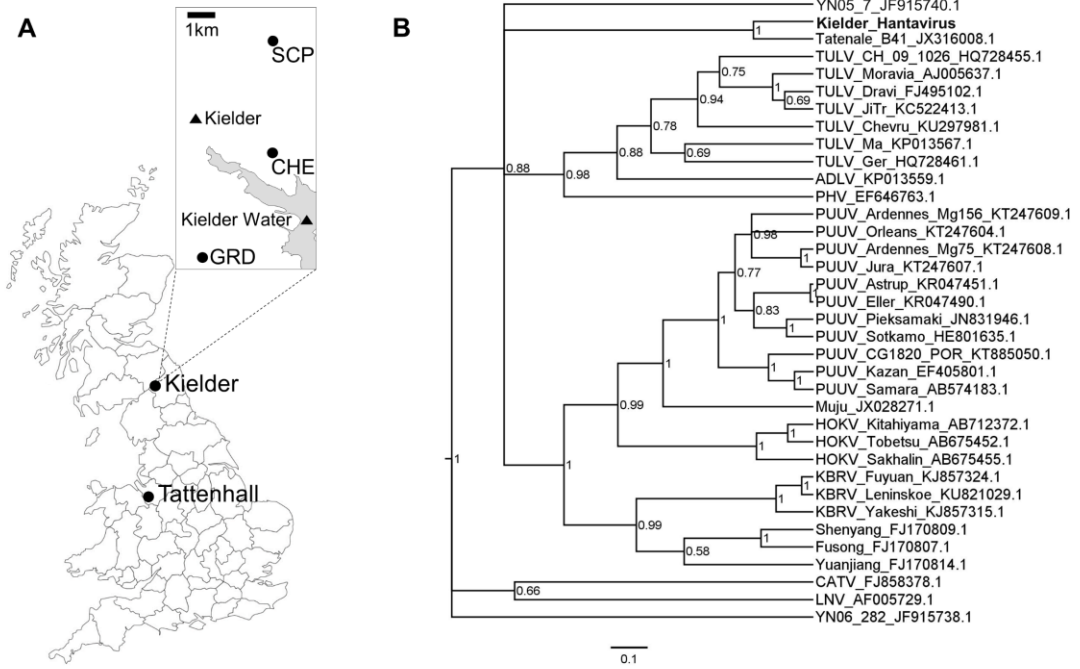
106 **Figure (main article) legend**

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108 Figure. (A) Map of mainland U.K. showing localities for Tatenale virus-like hantavirus
109 lineages; original site at Tattenhall, Cheshire (1) and additional sites at Kielder,
110 Northumberland (GRD: 55° 11' 1.61" N, -2° 35' 3.05" W; CHE: 55°13' 8.39" N, -2° 32'
111 26.50" W; SCP: 55° 15' 44.18" N, -2° 32' 41.05" W). (B) Bayesian phylogenetic tree for the
112 hantavirus genomic L segment (318 bp fragment, with no missing data), showing
113 relationships amongst Tatenale virus-like lineages and other relevant lineages. Phylogenetic
114 analysis was conducted using a GTR G+I model within *MrBayes* (9) software using Markov
115 chain Monte Carlo chain lengths of 1 million and a strict clock. Substitution models were
116 estimated using *MrModelTestV2* (10). The tree is drawn to scale with branch lengths
117 measuring the number of substitutions per site, and node values representing the posterior
118 probabilities. Scale bar represents 0.1 nucleotide substitutions per site. Sequences are
119 represented by the taxonomic names, strain (if more than one is included) and GenBank
120 ascension numbers. **Kielder_Hantavirus** represents the 145>A sequence found in this
121 study (the phylogeny is unchanged if the other sequence is substituted). ADLV, Adler Virus;
122 CATV, Catacamas Virus; HOKV, Hokkaido virus; KBRV, Khabarovsk virus; LNV, Laguna

123 Negra virus; PHV, Prospect Hill virus; PUUV, Puumala virus; TULV, Tula virus; YN05-YN06,
 124 unnamed hantaviruses.

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